I. STUDIES ON THE METAL-CATALYZED CYCLOADDITIONS OF ISOCYANATES AND UNSATURATED SYSTEMS AND II. CHROMIUM-CATALYZED SYNTHESIS OF 1,3-BUTADIENES VIA (SILYLMETHYL)ALLENES

A Dissertation

by

MARIA DURAN GALVAN

Submitted to the Office of Graduate Studies of
Texas A&M University
in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

August 2011

Major Subject: Chemistry

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Approved by:

Chair of Committee,	Brian T. Connell
Committee Members,	Daniel Romo
	Daniel A. Singleton
	Miguel A. Mora
Head of Department,	David H. Russell

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ABSTRACT

I. Studies on the Metal-Catalyzed Cycloadditions of Isocyanates and Unsaturated Systems and II. Chromium-Catalyzed Synthesis of 1,3-Butadienes via (Silylmethyl)allenes. (August 2011)

María Durán Galván, B.S., Instituto Tecnológico y de Estudios Superiores de Monterrey, Mexico

Chair of Advisory Committee: Dr. Brian T. Connell

Metal-catalyzed cycloadditions of alkynes with isocyanates or nitriles are valuable tools for the synthesis of complex carbocycles and heterocycles. Although this transformation has been studied for over three decades, the cyclizations of disocyanates with 1,3-dienes or allenes are not known and the asymmetric cycloadditions of isocyanates are scarce. To expand the scope of these powerful reactions, we studied the semi-intramolecular metal-catalyzed cycloaddition of several unsaturated systems with isocyanates. Our results show that further work in this area is needed to suppress the formation of undesired homo-coupled adducts and obtain the bicyclic products in a more efficient manner.

1,3-butadienes are versatile building blocks in organic synthesis. Therefore, it is our interest to develop an efficient method for their preparation making 1,3-butadienes more available for the organic chemist. A number of methods are known for the synthesis of these compounds, but the majority of them present problems such as poor regioselectivity, low atom economy, or require the use of toxic or non-readily available reagents. In order to develop a more effective synthesis, we employed (allenylmethyl)silanes as intermediates for the preparation of 1,3-butadienes utilizing (4-bromobut-2-ynyl)trimethylsilane as a diene equivalent.

A Nozaki-Hiyama-Kishi type transformation was used for the highly regioselective preparation of (trimethylsilyl)methylallenic alcohols from aldehydes and ketones. In addition, several tridentate bis(oxazolinyl)carbazole ligands were synthesized and used for the enantioselective synthesis of allenic alcohols. Carbazole ligands synthesis was achieved by the Suzuki coupling of carbazoles with different boronic acids followed by carbonylative amidation and cyclization. We report an efficient new method for the desilylation of allenic alcohols providing a variety of secondary and tertiary 1,3-butadienylcarbinols. Furthermore, our interest in extending this methodology led us to the discovery of a novel synthesis of 2-aminomethyl-1,3-dienes from *N*-tosyl imines.

Para mi familia.

Gracias por compartir mis sueños,

juntos los estamos haciendo realidad.

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My deepest gratitude and love go to my family for embracing my dreams and working together with me to make them come true. Thank you for your infinite help, valuable life lessons and for always believing in me. To my mother, Zoila Galván, thank you for teaching me the importance of having faith; you gave me the greatest lesson in courage when you defeated cancer. To my father, Ismael Durán, with your example you taught me to work very hard and have discipline. I admire you both. I want to thank my brother, Mauricio Durán, bold dreamer, who taught me not to be afraid of the unknown; you bid me to pursue great ambitions. Finally, to the memory of my beloved grandmother: you still comfort me through fond memories and dreams.

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1. INTRODUCTION TO THE METAL-CATALYZED CYCLOADDITIONS OF ISOCYANATES

1.1. Background

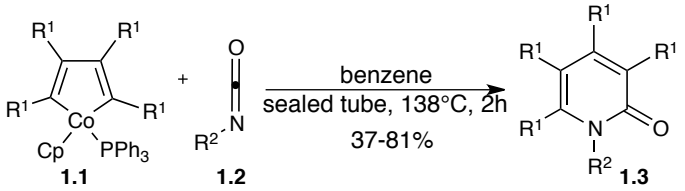
Metal-catalyzed cycloadditions have shown to posses immense value in the synthesis of complex carbocycles and heterocycles that can potencially be used in the total synthesis of natural products.[1] Particularly, the cycloaddition of alkynes to isocyanates or nitriles can be a powerful tool in the synthesis of nitrogen containing heterocycles such as pyridines and pyridones.[2] These atom economic transformations allow the formation of multiple carbon-carbon bonds in one step with high regio- and chemoselectivity.

Although Yamazaki and Hong reported the first example of a metal-mediated cycloaddition involving isocyanates in 1977,[3] only few methodologies have thus far been developed. Moreover, the majority of the reports published to date include the inter- or intramolecular [2+2+2] cycloaddition of alkynes to isocyanates, and only two asymmetric cycloadditions of isocyanates have been reported. Some of the first transformations required high temperatures to give the desired product usually in low to moderate yields. These seminal reports are described below.

In the intermolecular cobalt(I)-mediated cycloaddition reported by Yamazaki and Hong[3], cobalt cyclopentadiene complex **1.1** was reacted with an isocyanate species to produce pyridones **1.3** in 37-81% yields. Temperatures as high as 130 °C were required for the cycloaddition to take place. (Scheme 1.1)

This dissertation follows the style of the *Journal of the American Chemical Society*.

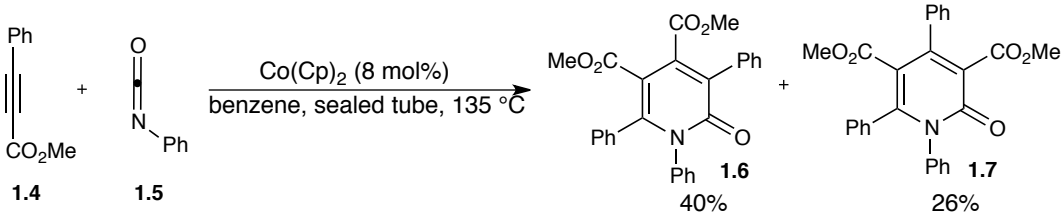
Scheme 1.1. Cobalt (I)-mediated synthesis of pyridones.



R^1=Ph, CO_2CH_3, CH_3 R^2=Ph, CH_3, nBu
Cp=cyclopentadienyl

Yamazaki and Hong subsequently reported the first cobalt-catalyzed [2+2+2] cycloaddition of isocyanates with several acetylenes to obtain pyridones **1.6** and **1.7**.[3] As depicted in Scheme 1.2, a mixture of regioisomers was obtained when unsymmetrical alkynes were employed giving moderate yields.

Scheme 1.2. Cobalt-catalyzed cycloaddition of phenylisocyanate with alkynes.

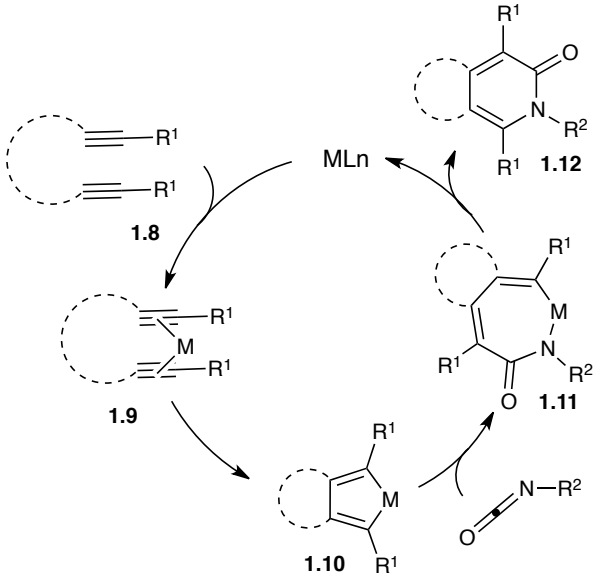


The cobalt-catalyzed [2+2+2] cycloaddition seems to follow the general mechanism shown in Scheme 1.3. First, the metal coordinates with two alkyne molecules or one diyne forming **1.9**. Next metallacyclopentadiene **1.10** is formed via an oxidative coupling. In the following step, the intermediate coordinates to an isocyanate, and after a migratory insertion the seven-membered ring **1.11** is formed. Finally, a reductive elimination occurs to give the desired pyridone **1.12** and to regenerate the catalyst. This mechanism can be applied to [2+2+2]

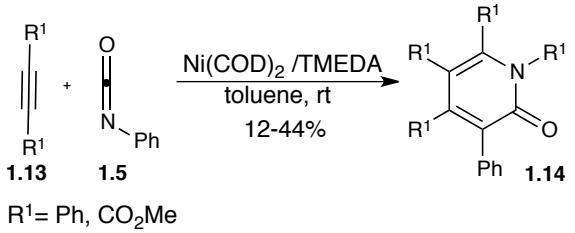
cycloadditions catalyzed by other metals such as rhodium, ruthenium and nickel with the corresponding modifications depending on the reaction conditions.[4]

In addition to cobalt, nickel was also one of the first metals used in an isocyanate cycloaddition. Hoberg and Oster developed a nickel(0)-mediated [2+2+2] cycloaddition between phenyl isocyanate and different alkynes to afford the corresponding pyridones **1.14.** (Scheme 1.4)[5] This cycloaddition required milder conditions than the work developed by Yamazaki *et al*. Unfortunately, the yields obtained were only in the range of 12 to 44%.

Scheme 1.3. Mechasnim for the cobalt-catalyzed cyclization of isocyanates.

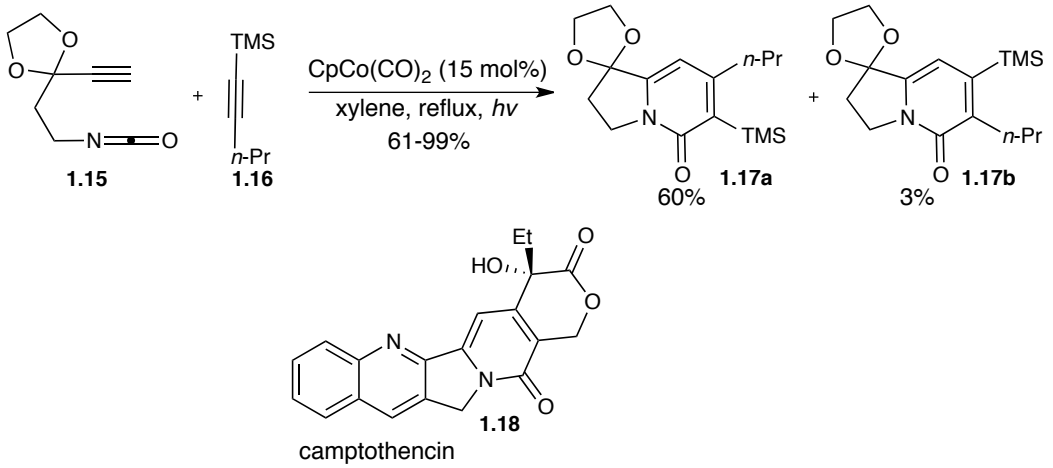


Scheme 1.4. Nickel-catalyzed synthesis of pyridones.



The first partially intramolecular [2+2+2] cycloaddition of 5-isocyanatoalkynes **1.15** to alkynes was achieved by Vollhardt and Earl[6] using $CpCo(CO)_2$ as a catalyst. High regeoselectivity is observed during this transformation due to the preference of the silyl group in the alkyne to be located adjacent to the carbonyl group. Vollhardt and Earl applied this methodology in a formal total synthesis of the antitumor agent camptothencin **1.18** (Scheme 1.5).[7]

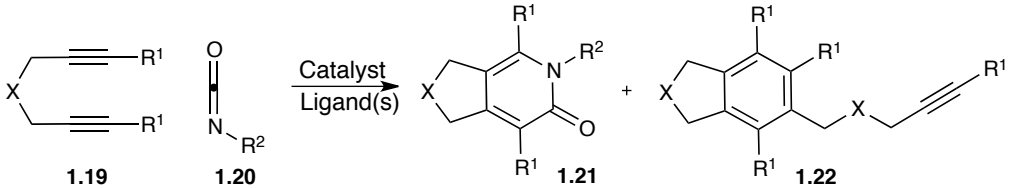
Scheme 1.5. Cycloaddition of 5-isocyanatoalkynes with alkynes



Pioneering work of Yamazaki, Hong and Vollhardt established the foundation for the development of different methodologies for the metal-catalyzed cyclization of isocyanates. Recently, the scope of the metal-catalyzed cycloadditions of isocyanates has expanded and procedures utilizing milder conditions while obtaining higher yields and better regioselectivity have been reported. The cycloaddition of symmetric 1,6-diynes **1.19** with isocyanates has become one of the most extensively studied transformations in this area, since the utilization of diynes allows the reduction in the regioselectivity problems plaguing intermolecular

cycloadditions. (Scheme 1.6) Itoh, Maryanoff, Loui and Tanaka have independently accomplished these novel cycloadditions by using ruthenium, nickel, cobalt and rhodium catalysts.

Scheme 1.6. General scheme for the metal-catalyzed synthesis of pyridones.



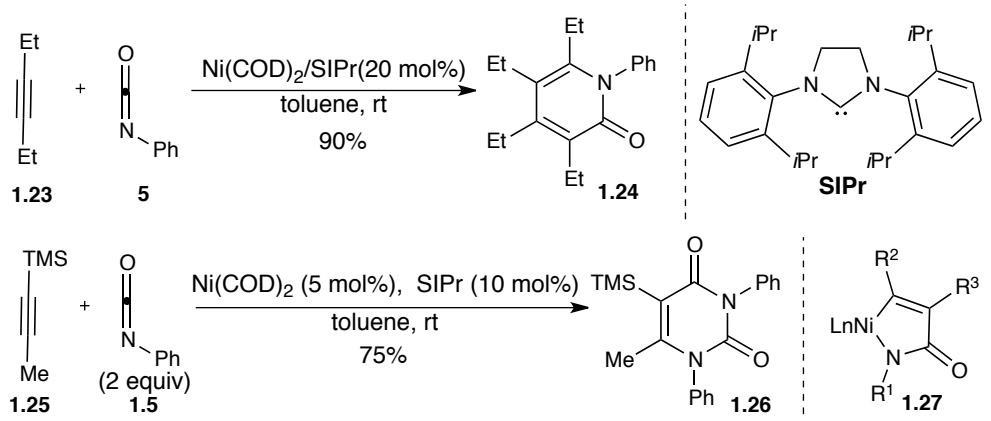
R_1= Me, *i*Pr, Et, H
R_2= Ph, Cy, Bu, Bn
X=$CH_2(CO_2Me)$, NTs, O, C_2H_4

In 2001, Itho and co-workers reported the cycloaddition of α,ω-diynes **1.19** (R_1=H) with isocyanates to produce bicyclic pyridones **1.21.** This transformation was accomplished in the presence of a catalytic amount of Cp*Ru(COD)Cl[8] in 1,2-Dichloroethane under reflux. (COD = 1,5cyclooctadiene, Cp*=η^5-C_5Me_5) The use of this ruthenium catalyst allowed the formation of pyridones under mild conditions and with good yields (58-93%) following the mechanism depicted in Scheme 1.3. However, the competing dimerization of the diyne **1.19** to form the aromatic compound **1.22** was also observed. This side reaction was suppressed by dropwise addition of the diyne to a solution of the catalyst and the corresponding isocyanate in 1,2-dichloroethane. Similarly, Marianoff reported the $CpCo(CO)_2$ catalyzed cyclization of α,ω-diynes with isocyanates to form macrocylic pyridones in 30-65% yields.[9]

Louie *et al*. developed the nickel(0)-catalyzed partially intramolecular cycloadditions. In this report, internal 1,6-diynes were coupled with aryl and alkyl isocyanates to produce the desired pyridones **1.21** in 61-99% yield.[10] The reaction conditions were optimized using

$Ni(COD)_2$ as a source of nickel(0) in toluene at room temperature and N-heterocyclic carbenes, such as SIPr, as ligands. In this case, the undesired dimerization reaction that leads to **1.22** was not observed under the optimized reaction conditions. In addition to the intramolecular reaction described above, Louie and co-workers achieved the intermolecular cyclization of isocyanates and alkynes. As shown in Scheme 1.7, when 3-hexyne was mixed with phenyl isocyanate in the presence of $Ni(COD)_2$/SIPr, the corresponding pyridone **1.24** was obtained in 90% yield.[10] Nevertheless, when a large excess of phenyl isocyanate is used, a mixture of products is observed. In this case, pyrimidine-diones **1.26** are obtained as the minor product. Furthermore, when more hindered alkynes are used (such as 1-trimethylsylil-1-propine **1.25**) pyrimidine-diones are obtained as a single product.[11]

Scheme 1.7. Nickel-catalyzed cycloadditions of phenylisocyanate and alkynes.



These observations concur with the mechanism previously proposed by Hoberg and Oster,[5] in which the nickel catalyst reacts with one molecule of isocyanate and one alkyne to form intermediate **1.27,** instead of the proposed metallacycle for the cobalt or ruthenium

catalyzed reactions. (Scheme 1.3). Such an intermediate can follow two different paths reacting either with an isocyanate or with an alkyne moiety. When the isocyanate is present in excess and the substituents in the alkyne are bulky, the insertion of another molecule of isocyanate is favored versus the insertion of the alkyne and dione **1.26** is formed. Steric effects have an important role in this transformation due to the presence of bulky ligands such as SIPr.[11]

Tanaka and co-workers have developed a number of [2+2+2] cycloadditions catalyzed by the cationic rhodium complex $[Rh(COD)_2]BF_4$ and BINAP-type ligands such as H8-BINAP (Figure 1.1). Although the main focus of this research group has been the development of enantionselective [2+2+2] cycloadditions of alkynes they have also reported heterocycloadditions with nitriles, isocyanates and thioisocyanates.[12] One of these examples involves the [2+2+2] cycloaddition of 1,6-diynes with isocyanates catalyzed by $[Rh(COD)_2]BF_4$/ H8-BINAP in dichloromethane at room temperature.[13] Similar to the methodologies developed by Itoh and Louie, this reaction can take place with aryl, alkyl, or cyclohexyl isocyanates; additionally, terminal or internal diynes can be used for this transformation. (Scheme 1.6)

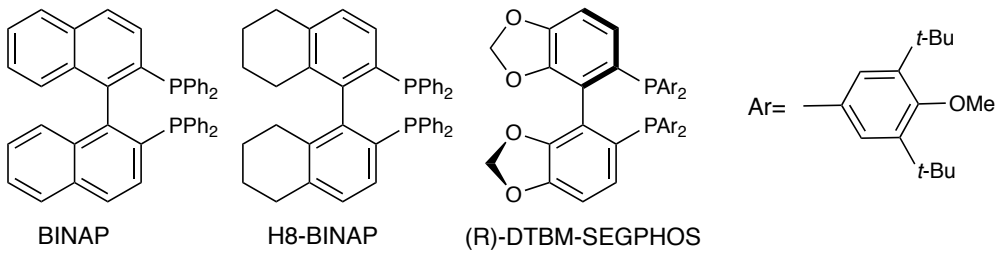
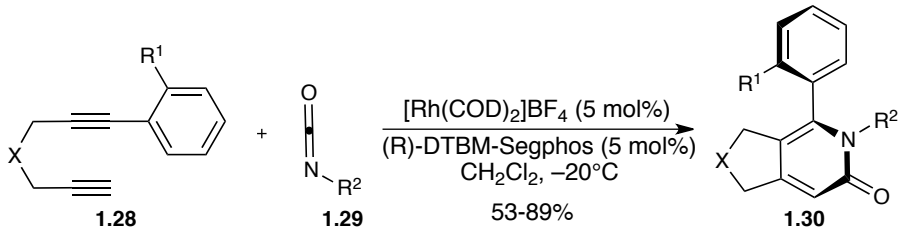


Figure 1.1. Bidented phosphine ligands.

Tanaka *et al*. also developed the reaction of unsymmetrical diynes **1.28** with isocyanates to create axially chiral pyridones **1.30**. The transformation was achieved in the presence of

$[Rh(COD)_2]BF_4$ and (*R*)-DTBM-SEGPHOS (Figure 1.1) in good yields and high enantionselectivity as shown in Scheme 1.8. This constitutes the first enantioselective cycloaddition of isocyanates.

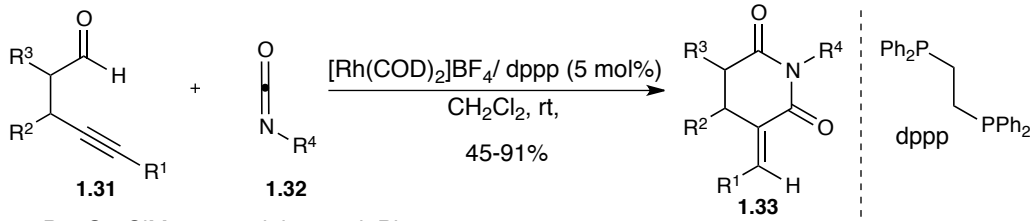
Scheme 1.8. Rhodium-catalyzed synthesis of axially chiral pyridones.



R^1=Cl, Br
R^2=Bn, *n*-Bu, *n*-C_8H_{17}
X=CH_2, O, $C(CO_2Me)_2$

An additional report from Tanaka and co-workers describes the first semi-intramolecular [4+2] cycloaddition of 4-alkynals with isocyanates to form six-membered heterocycles.[14] (Scheme 1.9) This transformation was accomplished in the presence of $[Rh(COD)_2]BF_4$ as a catalyst and dppp (1,3-bis(diphenylphosphino)propane) as a ligand in dichlorometane at room temperature.

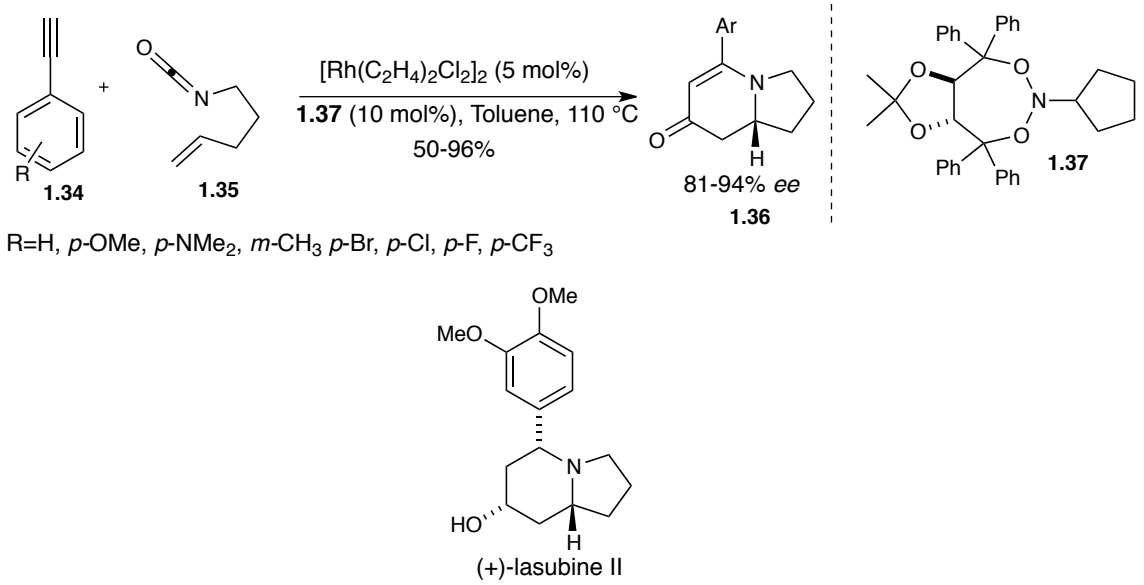
Scheme 1.9. Cycloaddition of 4-alkynals with isocyanates.



R_1=*n*-Bu, Cy, $SiMe_3$, 1-cyclohexenyl, Ph
R_2, R_3=Me, H
R_4=*n*-Bu, *n*-Oct, Bn, 4-MeOBn, Ph, Cy

All the cycloadditions discussed thus far involve the cyclization of isocyanates with alkynes to give unsaturated products. Consequently, the formation of a sp^3-chiral center was not observed. Nevertheless, Yu and Rovis were able to achieve the enantioselective [2+2+2] cycloaddition of alkenyl isocyanates with alkynes.[15] The use of an olefin allows the formation of a stereogenic center resulting in an enantioselective transformation accomplished in the presence of $[Rh(C_2H_4)_2Cl_2]_2$ and the chiral taddol derivate **1.37** as a ligand. Yet the expected lactam was observed only in small amount, or not at all. Instead, the vinilogous amide **1.36** was obtained. This methodology was successfully applied to the total synthesis of (+)-lasubine II (Scheme 1.10).

Scheme 1.10. Enantioselective rhodium-catalyzed cycloaddition of isocyanates and olefins.

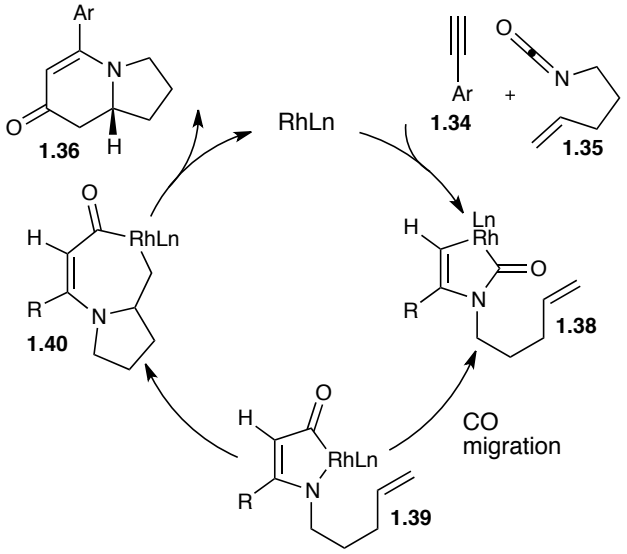


The formation of amide **1.36** can be explained by the proposed mechanism depicted in Scheme 1.11. After formation of the rhodium methalacycle, a CO migration occurs to give the

intermediate **1.39,** which after a migratory insertion and a reductive elimination gives the observed vinylogous amide.

It can be observed that many highly efficient methods for the cyclization of isocyanates have been developed. Most of the transformations reported to date involve the [2+2+2] cyclization of isocyanates to alkynes and, unfortunately, the employment of other pi-systems is reduced. Furthermore, only two enantioselective reactions have been achieved. It can also be noted that, in most cases, better selectivity and yields are obtained with semi-intramolecular cyclizations. Hence, in order to expand the scope and utility of isocyanate cycloadditions, it was envisioned that isocyanates could react with functional groups other than alkynes (such as dienes, allenes and vinyl cyclopropanes) to generate heterocyclic products containing at least one stereogenic center.

Scheme 1.11. Mechanism for the synthesis of vinilogous amide **1.36.**

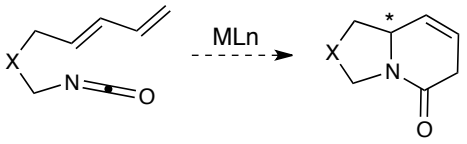


1.2. Results and discussion

1.2.1. Intramolecular [4+2] cycloadditions of isocyanates with dienes

Our initial efforts were focused towards the intramolecular cycloaddition of dienes with isocyanates. Having in mind the well known metal-catalyzed [4+2] cyclization of dienes with alkynes and allenes[16] it was pictured that, utilizing isocyanates, this process could lead to six-membered heterocycles. It is anticipated that the resulting bicylic amides will contain bridgehead nitrogen and one chiral center. (Scheme 1.12)

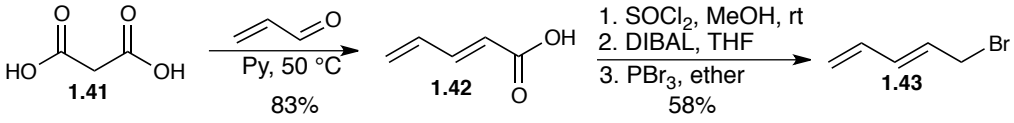
Scheme 1.12. Proposed synhtesis of bicyclic amides.



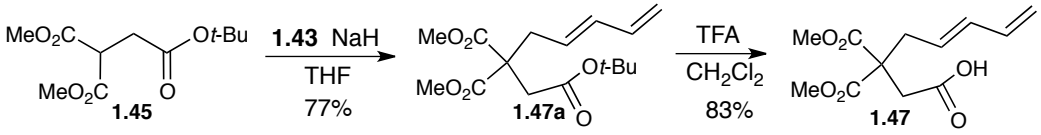
In order to explore this transformation, isocyanate **1.48** was synthesized from the known aldehyde **1.46**. As described in Scheme 1.13, 2,4 pentadienoic acid was obtained by the reaction of malonic acid with acrolein following decarboxylation by the procedure reported by Liang *et al*.[17] Esterification of 2,4-pentadienoic acid, followed by DIBAL reduction and bromination provided 5-bromopenta-1,3-diene **1.43**.[18] The bromide was then mixed with **1.45**[19] in the presence of sodium anhydride to afford the corresponding *tert*-butyl ester **1.47a** in 77% yield (Scheme 1.14). Next, the *tert*-butyl protecting group was removed in the presence of trifluoroacetic acid to give the desired acid in 83% yield. Although this method afforded the desired compound in good yield, the acid was not obtained in high purity. An alternative route is described in Scheme 1.15. Dimethyl 2-(2,2-dimethoxyethyl)malonate **1.45,** obtained from the

alkylation of dimethyl malonate with 2-bromo-dimethoxyethane,[20] was alkylated with 5-bromopenta-1,3-diene. The product of the alkylation was then deprotected with ferric trichloride to obtain the corresponding aldehyde.[21] Subsequently, aldehyde **1.46** was successfully oxidized to the acid under Pinnick oxidation conditions in quantitative yield. Acid **1.47** was treated with ethyl chloroformate to form a mixed anhydride from which, upon treatment with sodium azide, the corresponding acyl azide was obtained. Finally, Curtius rearrangement of the generated acyl azide provided the desired isocyanate in 43% yield.

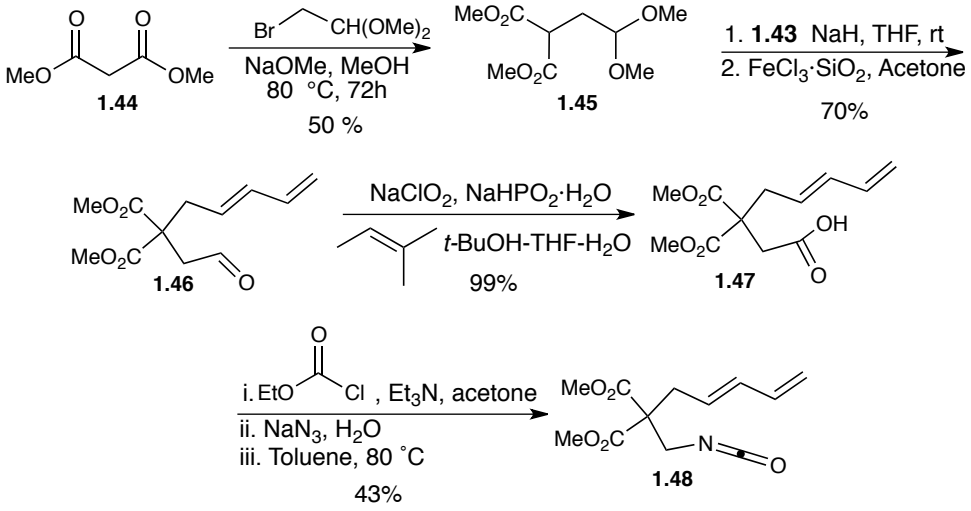
Scheme 1.13. Synthesis of 5-bromopenta-1,3-diene.



Scheme 1.14. Synthesis of 3,3-bis(methoxycarbonyl)octa-5,7-dienoic acid

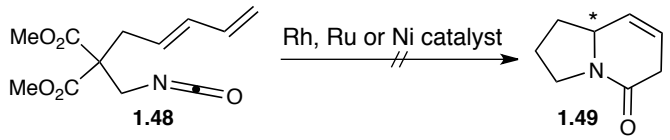


Scheme 1.15. Synthesis of dimethyl 2-(isocyanatomethyl)-2-(penta-2,4-dien-1-yl)malonate.



With the desired isocyanate prepared, the intramolecular [4+2] cyclization was studied. Unfortunately, no cycloadduct was observed in presence of rhodium catalyst. Furthermore, catalytic systems known to be highly reactive towards isocyanates, such as $Ni(COD)_2$/SIPr, $[Rh(COD)_2]BF_4$/H8-BINAP and Ru(COD)Cp*, did not afford the desired product (Scheme 1.16).

Scheme 1.16. Metal-catalyzed attempted synthesis of bicyclic amides.



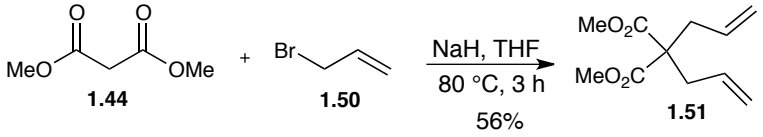
1.48 **1.49**

Catalyst = $[Rh(COD)_2]BF_4$, $[Rh(COD)_2Cl]_2$,
$Ni(COD)_2$/SIPr, $[Rh(COD)_2]BF_4/H_8$-BINAP, Ru(COD)Cp*

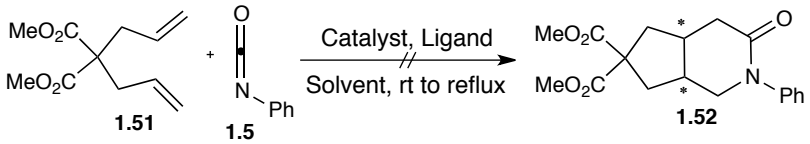
1.2.2. Attempted [2+2+2] cycloaddition of phenyl isocyanate with diallylmalonate

Aiming for a cyclization that could lead to saturated pyridones, it was envisioned that bicyclic amides containing two stereogenic centers could be prepared by a [2+2+2] cyclization of isocyanates with olefins. The use of symmetric substrates during a semi-intermolecular cycloaddition will eliminate possible regioselectivity problems. The required substrate was synthesized by the alkylation of dimethyl malonate with allyl bromide in the presence of sodium hydride.[22] (Scheme 1.17) Unfortunately, malonate **1.51** proved to be unreactive toward cyclization with phenyl isocyanate under several conditions (Scheme 1.18).

Scheme 1.17. Synthesis of dimethyl 2,2-diallylmalonate.



Scheme 1.18. Attempted cyclization of dimethyl 2,2-diallylmalonate with phenylisocyanate.



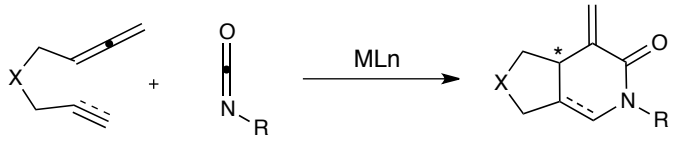
Catalyst= $Ru(COD)Cp^*Cl$, $Ni(COD)_2$, $[Rh(COD)_2]BF_4$, $[Rh(COD)_2Cl]_2$, $[Rh(C_2H_4)_2Cl]_2$, $[RhCl(CO)_2]_2$
L= IPr, BINAP, dppe, $P(OPh)_3$, Monophos
Solvent= DCE, CH_2Cl_2, toluene

At this point, our attention was focused in finding more reactive substrates that could also lead to saturated amides such as **1.52**. It was envisioned that allenes could be used for this transformation, expecting a higher reactivity than olefins under this conditions.

1.2.3. Synthesis and [2+2+2] cycloaddition of allenes with isocyanates

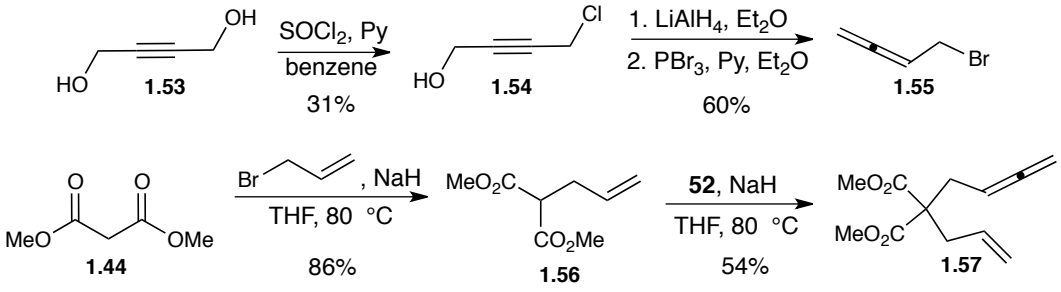
Allenes are known to undergo [2+2+2] cycloaddition reactions with alkynes in the presence of nickel[23] and cobalt-based[24] catalysts. In addition, the rhodium-catalyzed [2+2+1] cycloadditions of diene-allenes in CO atmosphere have been developed.[25] Based on this precedent, it was considered that alkenes or alkynes tethered to allenes could undergo [2+2+2] cycloadditions with isocyanates to yield the desired bicyclic amides and to form at least one stereogenic center, as depicted in Scheme 1.19.

Scheme 1.19. Proposed cyclization of allenes with isocyanates.



Allene **1.57** was synthesized following the procedures reported by Molander[26] and Itoh.[27] The commercially available but-2-yne-1,4-diol **1.53** was treated with thionyl chloride in the presence of pyridine to afford 4-chlorobut-2-yn-1-ol **1.54** in 31% yield. Compound **1.54** should be handled with caution since is a very strong irritant. Afterwards, **1.54** was reacted with lithium aluminum hydride and then phosphorus tribromide to provide 4-bromobuta-1,2-diene **1.55** in 60% yield. Dimethyl 2-(2-propenyl)malonate **1.56** was obtained from the alkylation of malonate with allyl bromide. Finally, allene **1.55** was used to alkylate **1.56** and the desired allene was obtained in 54% yield (Scheme 1.20).

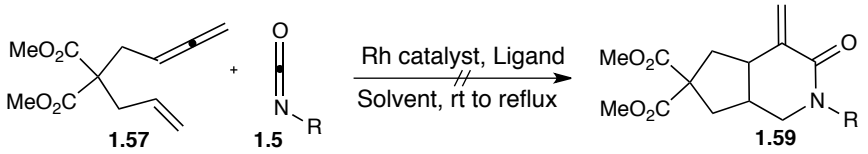
Scheme 1.20. Synthesis of dimethyl 2-allyl-2-(buta-2,3-dien-1-yl)malonate



Once compound **1.57** was synthesized, it was mixed with phenyl and benzyl isocyanates under numerous conditions. In the presence of a catalytic amount of rhodium complexes, such as $[Rh(COD)_2]BF_4$, $[Rh(COD)Cl_2]_2$ or $[Rh(C_2H_2)_2Cl]_2$, cyclopentane **1.58** was observed by ^1H

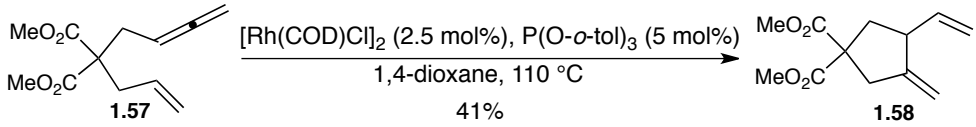
NMR analysis instead of the desired cycloadduct. The observed compound results from the competing intramolecular cycloisomerization of allene **57** (Scheme 1.21). As shown in Scheme 1.22, Makino and Itoh previously achieved this transformation in the presence of a catalytic amount of $[RhCl(COD)]_2$.[27]

Scheme 1.21. Attempted rhodum-catalyzed cyclization of dimethyl 2-allyl-2-(buta-2,3-dien-1-yl)malonate with isocyanates.



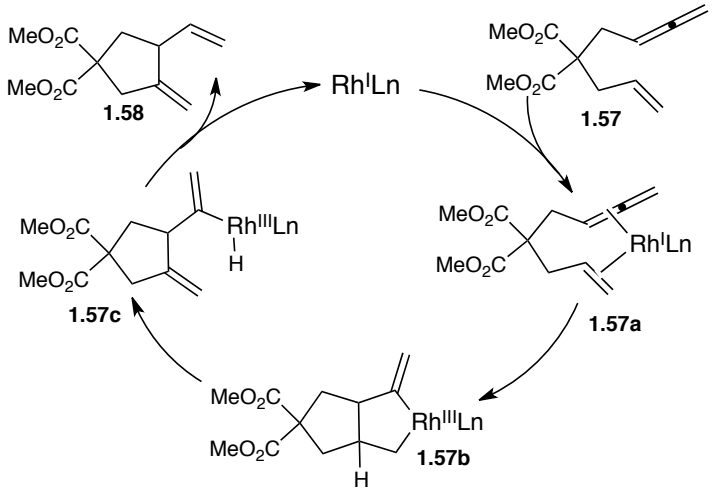
Catalyst= $[Rh(COD)_2]BF_4$, $[Rh(COD)Cl_2]_2$ or $[Rh(C_2H_2)_2Cl]_2$, $[RhCl(CO)_2]_2$
Ligands= BINAP, $P(OPh)_3$, Monophos
Solvent= DCE, toluene

Scheme 1.22. Intramolecular rhodum-catalyzed cyclization of dimethyl 2-allyl-2-(buta-2,3-dien-1-yl)malonate[27]



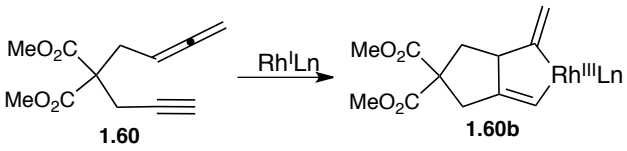
The formation of product **1.58** can be explained following the mechanism depicted in Scheme 1.23. To commence, a rhodium (I) complex coordinates at the allenic π-bond leading to the formation of intermediate **1.57a**. Next, oxidative cyclization affords metallacycle **1.57b,** which undergoes a β-hydride elimination of the hydrogen situated at the bridgehead position to afford the corresponding complex **1.57c**. Finally, metallacycle **1.57c** gives the desired compound by a reductive elimination process and the catalyst is regenerated.

Scheme 1.23. Mechanism for the rhodium-catalyzed cycloisomerization of allenes.[27]



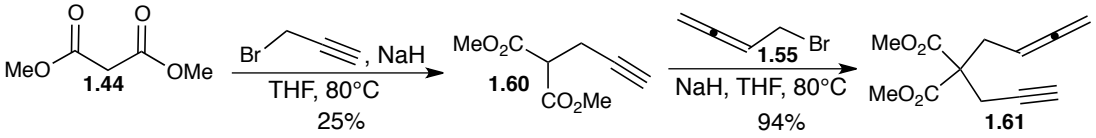
Because the [2+2+2] cycloaddition of isocyanates with alkynes is very well documented, it was decided to exchange the olefin moiety in the substrate for an alkyne, This eliminates the possibility of an intramolecular cycloisomerization reaction due to the absence of a β-hydrogen in metallacycle **1.60b**. Thus, impeding the formation of the corresponding cycloadduct. (Scheme 1.24)

Scheme 1.24. Formation of metallacycle **1.60b**.



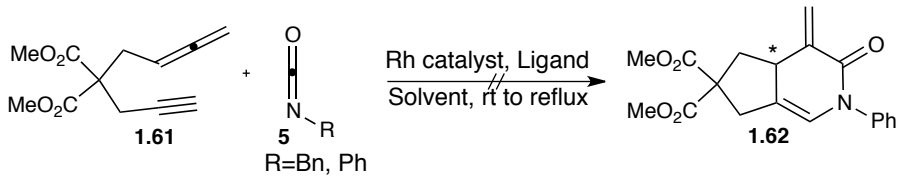
As shown in Scheme 1.25, the synthesis of the terminal alkyne **1.61** was accomplished by alkyation of dimethyl malonate **1.44** with propargyl bromide, and a subsequent alkylation with 4-bromobuta-1,2-diene **1.55**, which provided the desired tethered allene in 96% yield.

Scheme 1.25. Synthesis of dimethyl 2-(buta-2,3-dien-1-yl)-2-(prop-2-yn-1-yl)malonate.



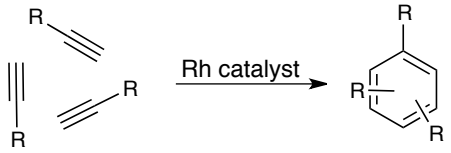
Having prepared the tethered alkylallene **1.61**, it was mixed with phenyl and benzyl isocyanates in the presence of different rhodium complexes. Although the starting material was consumed, the desired pyridone was not obtained. (Scheme 1.26) It is hypothesized that compound **1.61** could have dimerized. Homo-coupled products have been previously identified in [2+2+2] cycloadditions with terminal alkynes (See Scheme 1.6).[8b] In addition, the formation of aromatic compounds resulting from the known alkyne cyclotrimerization is also possible (Scheme 1.27).[28]

Scheme 1.26. Attempted cyclization of **1.61** with isocyanates.



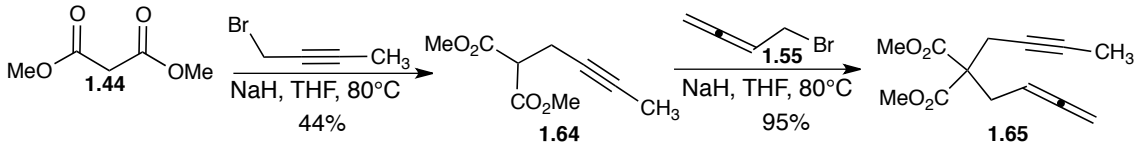
Catalyst = $[Rh(COD)_2]BF_4$, $[Rh(COD)_2Cl]_2$, $[Rh(C_2H_4)_2Cl_2$, $[RhCl(CO)_2]_2$
L=BINAP, dppe, $P(OPh)_3$, Monophos
Solvent= 1,2 DCE, toluene

Scheme 1.27. Cyclotrimerization of alkynes. [28]



Previous reports of nickel-catalyzed cyclizations of isocyanates with internal 1,6-diynes describe the synthesis of 2-pyridones suppressing the formation of the undesired diyne dimer or trimer[10]. Therefore, it was speculated that a different outcome might be obtained by utilizing internal alkynes. In order to explore this possibility, internal alkyne **1.65** was synthesized by alkylation of dimethylmalonate giving the corresponding product **1.64** in 44% yield. To complete the synthesis malonate **1.64** was alkylated with allene bromide **1.55** in 92% (Scheme 1.28).

Scheme 1.28 Synthesis of dimethyl 2-(but-2-yn-1-yl)-2-(buta-2,3-dien-1-yl)malonate.



Interestingly, preliminary results show the cycloaddition of alkyne **1.65** to isocyanates in the presence of $[Rh(COD)_2]BF_4$ and BINAP, produced pyridone **1.67** whose can be explained by the isomerization of the expected product **1.66**, as shown in Scheme 1.29. The synthesis of pyridone **1.67** was previously achieved by the nickel-catalyzed cyclization of diyne **1.19** with phenylisocyanate and described in Scheme 1.6. In addition, a major by-product was identified by mass spectroscopy as the homo-coupled adduct of **1.65**. A plausible structure for this adduct is shown in Figure 1.2, anticipating the favored formation of an aromatic adduct as it as been observed in previous metal-catalyzed cyclization reactions involving alkynes.[8b] Pyridone **1.67** and the homo-coupled product were isolated in a 1:1 ratio.

With this promising result, it was decided to study the cycloaddition of disubstituted allenes, aiming to avoid the isomerization of the desired product and not to lose the sterogenic center in the pyridone. To accomplish this, allene **1.70** was synthesized as described in Scheme 1.30. First, following the procedure reported by Cook and Danishefsky,[29] 1-bromo-2-butyne was mixed with formaldehyde in the presence of indium to obtain the corresponding allenyl alcohol. After that, the alcohol was brominated with PBr_3 to give allene bromide **1.69**, which was utilized to alkylate malonate **1.64** and complete the synthesis of the desired disubstituted allene.

Scheme 1.29. Rhodium-catalyzed cyclization of **1.61** with phenylisocyanate.

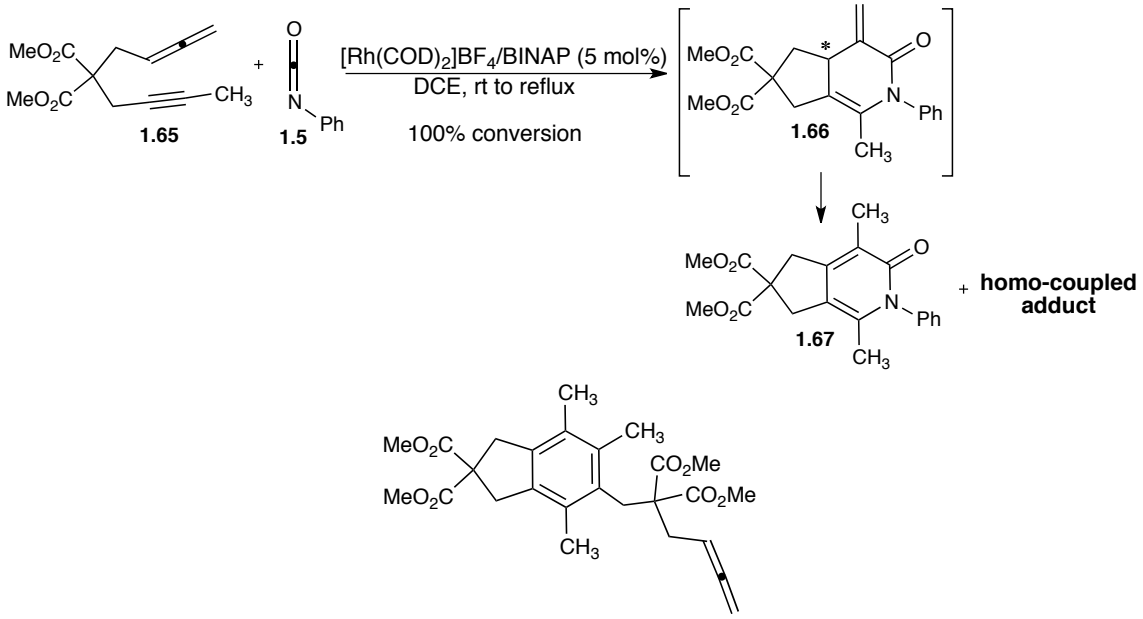
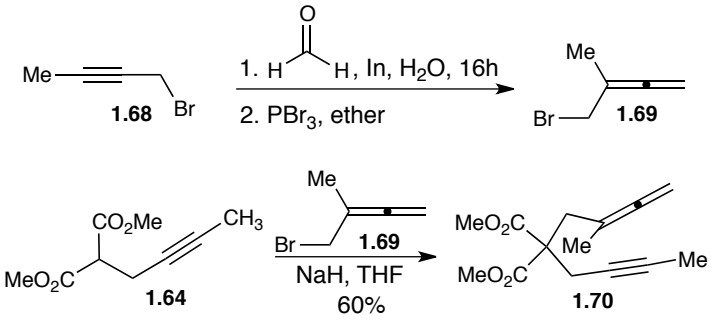


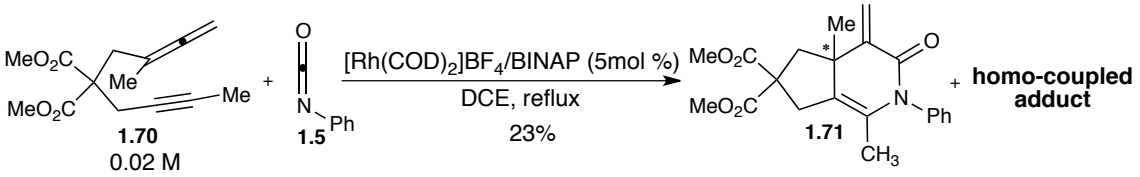
Figure 1.2. Homo-coupled adduct of alkyne **1.65**.

Scheme 1.30. Synthesis of dimethyl 2-(but-2-yn-1-yl)-2-(2-methylbuta-2,3-dien-1-yl)malonate.

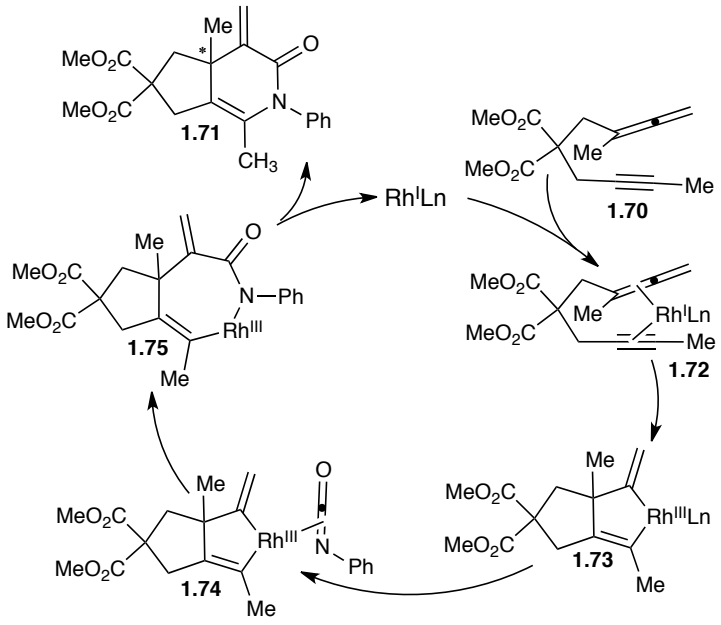


Preliminary results showed that mixing 1.70 with phenyl isocyanate in presence of $[Rh(COD)_2]BF_4$/BINAP afford the desired amide **1.71** (Scheme 1.31). The presence of the amide was determined by crude ^1H NMR and mass spectroscopy. The desired amide was also obtained using benzyl isocyanate. Formation of the desired adduct can be explained by the mechanism depicted in Scheme 1.32. After the rhodium catalyst coordinates to the p-system of the allene and alkyne, intermediate **1.72** undergoes an oxidative coupling to afford rhodium metallacycle **1.74**. Next, coordination to a molecule of isocyanate and migratory insertion give **1.75**. Finally, a reductive elimination occurs to afford bicyclic amide **1.71** and regenerate the catalyst. Unfortunately, further optimization, including lowering the concentration of the starting material and reducing the temperature of the reaction, did not increase the yield of the desired product. It can be deduced that the main product remains to be a homo-coupled adduct of **1.70**, identified by mass spectroscopy.

Scheme 1.31. Synthesis of bicyclic amide **1.71**.



Scheme 1.32. Pausible mechanism for the formation of **1.71**.

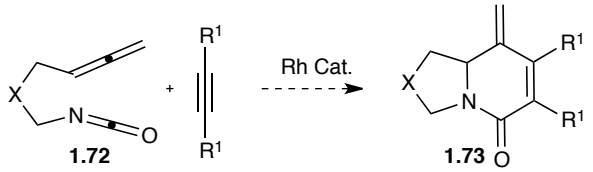


1.2.4. Enantioselective [2+2+2] cycloaddition allene-isocyanates with alkynes

Bicyclic compounds containing bridgehead nitrogen atoms are recurrent in numerous natural products such as alkaloids.[1b] Therefore, transformations capable to produce such moieties in an efficient manner have high synthetic value. It is our intention to develop a method from which six and seven-membered *N*-heterocycles can be obtained in an asymmetric fashion. The metal-catalyzed [2+2+2] cycloaddition of alkenylisocyanates and alkynylisocyanates with alkynes were independently achieved by Vollhardt[6] and Rovis.[15] These cyclizations provide bicyclic pyridones containing a bridgehead nitrogen which, as Vollhardt and Rovis have demonstrated, can be useful in the Total Synthesis of alkaloid Natural Products. Unfortunately, the methodology developed by Vollhardt only affords unsaturated pyridones (compound **1.17** in Scheme 1.5) and no chiral centers are generated. Considering these precedents and aiming to minimize possible regioselectivity problems in the cyclization of allenes with isocyanates we

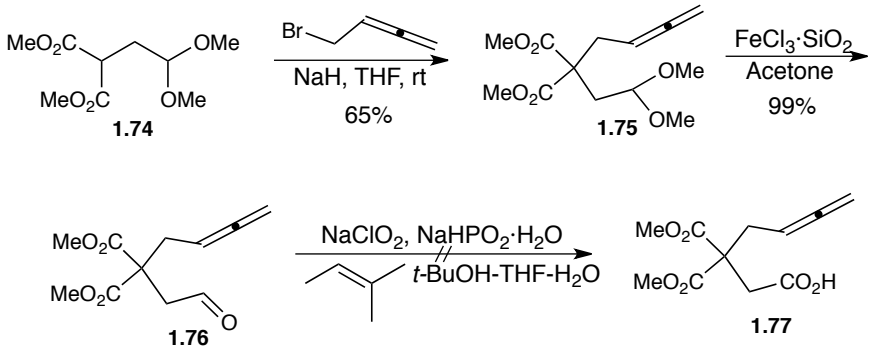
became interested in the development of a rhodium-catalyzed [2+2+2] cycloaddition of 1,7-alleneisocyanates with alkynes to yield bicyclic lactams. (Scheme 1.33)

Scheme 1.33. Proposed synthesis of bicyclic lactams.



The synthetic strategy followed for the preparation of allene-isocyanates **1.74** was similar to that of isocyanate **1.48** (Scheme 1.34). First, malonate **1.67**[20] was alkylated with 4-bromobuta-1,2-diene **1.47** to produce acetal **1.72**. Unfortunately, the desired acid was not obtained under Pinnick oxidation conditions. Thus this cyclization reaction was not explored.

Scheme 1.34. Towards the synthesis of 3,3-bis(methoxycarbonyl)hepta-5,6-dienoic acid.



1.3. Summary and conclusions

The metal-catalyzed [2+2+2] cycloaddition of alkynes and isocyanates is a powerful synthetic tool that has been extensively studied. Aiming to expand this methodology to the use of olefins and allenes, several cyclization substrates were synthetized.

Although the cyclization reactions were attempted under numerous conditions for a variety of substrates, the desired adducts were not obtained or were synthetized in poor yields. Olefin-containing substrates **1.48** and **1.51** proved to be unreactive towards cyclization in the presence of rhodium and, in the case of the latter, nickel and ruthenium catalyst.

On the other hand, cyclization reactions of allenes and alkynes were plagued with chemoselectivity problems. In the case of tethered alkene-allene **1.57**, only the product of a cycloisomerization reaction **1.58** was obtained. Compound **1.61** containing a terminal alkyne moiety did not afford the desired product. Is hypothesized that the corresponding homo-coupled product of **1.61** was formed.

Interestingly, tethered alkyne-allene **1.65** afforded an unsaturated pyridone, product of the isomerization of the expected compound. In an attempt to minimize the formation of undesired byproducts, methylallene **1.70** was synthetized and submitted to the cyclization conditions with phenyl isocyanate to afford the corresponding cycloadduct in 23% yield. Although the desired product was obtained, we were not able to increase the percent yield and the homocoupled product remained as the major adduct.

Finally, aspiring to the synthesis of pyridones containing a bridgehead nitrogen, the synthesis of thetered allene-isocyanates was attempted. Unfortunately, Pinnick oxidation of aldehyde **1.76** did not afford the corresponding acid, thus the synthesis of the desired isocyanate was not completed. Other conditions for the oxidation of **1.76** remain to be explored. Having

isocyanate **1.72** available will offer an exciting opportunity to study the semi-intramolecular reaction of isocyanates with allene and alkynes.

While the cyclization of isocyanates with alkynes and olefins can be achieved using different types of catalyst and conditions, additional studies to expand the scope of these transformations are needed. Further improvements that allow the asymmetric synthesis of saturated pyridones will be necessary to achieve the synthesis of more complex organic compounds. Such studies will increment the value of this transformation as a tool for the synthesis of nitrogen-containing natural products.

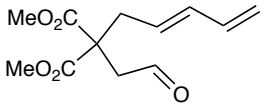
1.4. Experimental section

1.4.1. General information

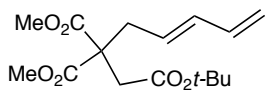
All reactions were performed under an argon atmosphere in oven-dried glassware with magnetic stirring. 1,2-dichloroethane was distilled from CaH_2 under an argon atmosphere before use. THF, CH_2Cl_2 and Toluene were dried with a solvent purification system. Other commercially available reagents were used as received. Reactions were monitored by analytical thin layer chromatography using 0.25 mm glass-backed silica gel plates. Flash column chromatography was performed using silica gel (230-400 mesh). Visualization was accomplished by UV light and potassium permanganate.

^{1}H NMR spectra were recorded at 300 MHz and referenced to $CDCl_3$ (δ 7.27). ^{1}H NMR coupling constants (*J*) are reported in Hertz (Hz) and multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dt (doublet of triplets), dd (doublet of doublets), ddd (doublet of doublet of doublets). Proton-decoupled ^{13}C NMR spectra were recorded at 75

MHz and reported relative to $CDCl_3$ (δ 77). Infrared Spectra were obtained as thin film on NaCl plates.

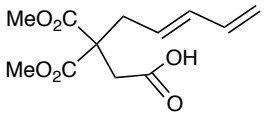


dimethyl-2-(2-oxoethyl)-2-(penta-2,4-dien-1-yl)malonate(1.46)[21]: Sodium hydride (72 mg of a 60% dispersion in mineral oil, 1.87 mmol) was added to a round bottom flask followed by addition of 150 mL of THF. Next, dimethyl 2-(2,2-dimethoxyethyl)malonate[30] **1.45** (330 mg, 1.5 mmol) was added slowly and the reaction mixture was stirred for 30 min. After this time, (*E*)-5-bromopenta-1,3-diene[31] (288 mg, 1.95 mmol) was added and the mixture was stirred at r.t for 2 h. A saturated solution of NH_4Cl was added to the mixture followed by extractions with diethyl ether (three times). The combined organic phases were dried over Mg_2SO_4 and concentrated under reduced pressure. The residue was pufiried by column chromatography (15% ethyl acetate in hexanes) to give the corresponding acetal as a clear oil (299 mg, 1.048 mmol, 70%). Then, the pure acetal was dissolved in acetone (26 mL) and $FeCl_3{\cdot}SiO_2$ (175 mg, 0.11 mmol) was added. The mixture was stirred for 1 h, filtrated though florisil and washed with ethyl acetate. The solvent was removed under recurred pressure and the residue was purified by column chromatography (15% ethyl acetate in hexanes) to give a clear oil (90 mg, 0.37, 70%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.7 (s, 1 H), 6.30 (ddd, *J* = 10.5, 10.5, 16.7 Hz, 1 H), 6.11 (dd, *J* = 10.5, 15.44 Hz, 1 H), 5.52 (dt, *J* = 7.58, 14.18 Hz, 1 H), 5.11 (d, *J* = 16.36 Hz, 1 H), 5.08 (d, *J* = 10.19 Hz, 1 H), 3.78 (s, 6 H), 3.01 (s, 2 H), 2.83 (d, *J* = 8.00 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.9, 170.6, 135.4, 136.1, 127.4, 117.5, 55.1, 53.2, 46.5, 37.4; IR (thin film) 2960.8, 1744.0, 1430.2, 1208.2 cm^{-1}; MS (ESI) calcd for $C_{12}H_{16}O_5$ (M + Li) 247.1158, found 247.1225.



(*E*)-1-*tert*-butyl 2,2-dimethyl hepta-4,6-diene-1,2,2-tricarboxylate (1.47a): Sodium hydride (2.1 g of 60% dispersion in mineral oil, 52.7

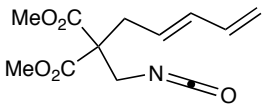
mmol) was added to a round bottom flask followed by addition of 150 mL of THF. Next, 2-*tert*-butyl 1,1-dimethyl ethane-1,1,2-tricarboxylate[19] (10.8 g, 44 mmol) was added slowly and the reaction mixture was stirred for 30 min. After this time, (*E*)-5-bromopenta-1,3-diene[31] (11 g, 81.8 mmol) was added and the mixture was stirred at 80 °C overnight. A saturated solution of NH_4Cl was added to the yellow mixture followed by extractions with diethyl ether (three times). The combined organic phases were dried over Mg_2SO_4 and concentrated under reduced pressure. The residue was purified with column chromatography (8-15% ethyl acetate in hexanes) to afford the desired compound (6.02 g, 19.2 mmol, 77%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.32 (ddd, *J* = 10.4, 10.4 17.4 Hz, 1 H), 6.12 (dd, *J* =10.9, 14.9 Hz, 1 H), 5.57 (dt, *J* = 7.9, 14.9 Hz, 1 H), 5.17 (d, *J* = 17.5 Hz, 1 H), 5.07 (d, *J* = 9.6 Hz, 1 H), 3.77 (s, 6 H), 2.9 (s, 2 H), 2.81 (d, *J* = 7.7 Hz, 2 H), 1.46 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0, 170.5, 136.4, 135.5, 127.5, 116.8, 81.2, 55.7, 52.7, 38.7, 36.6, 27.9; MS (ESI) calcd for $C_{16}H_{24}O_6$ (M + H) 313.1651, found 313.1756.



3,3-bis(methoxycarbonyl)octa-5,7-dienoic acid (1.47): Method 1: 1-*tert*-butyl 2,2-dimethyl hepta-4,6-diene-1,2,2-tricarboxylate **1.47a** (1.11 g, 3.5 mmol) was dissolved in CH_2Cl_2, After addition of trifluoroacetic acid (0.3 mL, 3.9 mmol), the mixture was stirred at r.t. for 3 hours. After this time more trifloroacetic acid was added (10.5 mmol) and the mixture was refluxed overnight. After cooling to room temperature, the solution was washed with brine and extracted with 3 portions of ethyl acetate. The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The desired compound was obtained as a clear oil (0.76 g, 2.96 mmol, 84%).

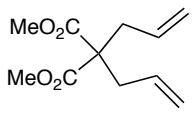
Method 2: dimethyl 2-(2-oxoethyl)-2-(penta-2,4-dien-1-yl)malonate[21] **1.46** (90 mg, 0.37 mmol), was dissolved in THF/*t*BuOH (2 mL). Then, 2-methyl-2-butene (1.15 mL, 11.07 mmol)

and NaH_2PO_4 (0.4 g, 2.9 mmol) were added to the mixture followed by a solution of $NaClO_2$ (100 mg, 1.11 mmol) in water (1 mL). The slightly yellow solution was stirred at r.t. for 5 h. After this time, $NaHCO_3$ was added and the mixture was acidified again with 1M HCl. Finally, the mixture was extracted with three portions of ethyl acetate, dried over Na_2SO_4 and concentrated under reduced pressure to afford a clear oil. The obtained product did not required further purification. (94 mg, 2.96 mmol, 99%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.28 (ddd, *J* = 10.5, 16.7 Hz, 1 H), 6.11 (dd, *J* = 10.5, 15.44 Hz, 1 H), 5.52 (dt, *J* = 7.58, 14.18 Hz, 1 H), 5.11 (dd, *J* = 1.56, 16.36 Hz, 1 H), 5.08 (dd, *J* = 1.49, 10.19 Hz, 1 H), 3.76 (s, 3 H), 3.01 (s, 2 H), 2.83 (d, *J* = 8.00 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.7, 170.5, 136.5, 136.1, 127.3, 117.5, 55.7, 53.2, 37.3, 37.0; IR (thin film) 2962.8, 1736.6, 1434.9 cm^{-1}; MS (ESI) calcd for $C_{12}H_{16}O_6$ (M - H) 255.0874, found 255.0810.

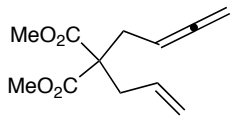


dimethyl-2-(isocyanatomethyl)-2-(penta-2,4-dien-1-yl)malonate (1.48): Acid **1.47** (590 mg, 2.3 mmol) was dissolved in acetone (10 mL) and cooled to 0 °C. Then, Et_3N (0.35 mL, 2.5 mmol) is added to the solution and a white precipitate is formed. A solution of ethyl chloroformate (0.24 mL, 2.45 mmol) in acetone (1 mL) is added to the reaction solution dropwise. The mixture is stirred at 0°C for 45 minutes. After this time, a solution of sodium azide (0.3 g, 4.6 mmol) in H_2O (1 mL) is added and the mixture is stirred for 3 hours. The pink mixture was poured into ice water (60 mL) and extracted with toluene (3 portions of 80 mL). The combined organic phases were dried over Na_2SO_4. The resulting yellow solution was heated to reflux, bubbling was observed starting at 80°C for at lest 30 min. The mixture was refluxed for two hours and toluene was removed to afford a yellow oil 90% pure (150 mg, 0.6 mmol, 45%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.27 (ddd, *J* = 10.2, 10.2, 16.8 Hz, 1 H), 6.11 (dd, *J* = 10.47, 14.5 Hz, 1 H), 5.54 (dt, *J* = 7.88, 14.75 Hz, 1 H), 5.11 (d, *J* =

16.6 Hz, 1 H), 5.04 (d, *J* = 10.5 Hz, 1 H), 3.74 (s, 6 H), 3.64 (s, 2 H), 2.71 (d, *J* =7.57 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 136.4, 129.3, 128.4, 126.4, 117.7, 58.5, 53.2, 44.9, 34.8; IR (thin film) 3037.8, 2264.3, 1717.4, 1492 cm^{-1}; MS (CI) calcd for $C_{12}H_{15}NO_5$ (M + H) 254.10, found 254.2.

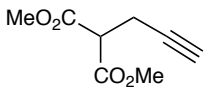


dimethyl 2,2-diallylmalonate (1.51)[22]: Sodium hydride (2.2 g of 60% dispersion in mineral oil, 92 mmol) was dissolved in THF (100 mL). Dimethyl malonate (2.6 mL, 23 mmol) was added dropwise at 0 °C and the solution was stirred for 1hr. Allyl bromide (8.8 mL, 103.5 mmol) was then added and the mixture was refluxed for 3 h. After cooling to r.t., the mixture was poured into a saturate solution of NH_4Cl and it was extracted with three portions of ether. The combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure to afford a yellow oil. The residue was purified by column chromatography (15% ethyl acetate in hexanes) to afford the desired compound as a clear oil (2.72 g, 12.7 mmol, 56%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.76-5.61 (m, 2 H), 5.17 (m, 2H), 5.12 (m, 2 H), 3.75 (s, 6 H), 2.68 (dt, *J* = 1.25, 7.30 Hz, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 132.2, 119.0, 57.5, 52.2, 36.8; MS (CI) calcd for $C_{11}H_{16}O4$ (M + H) 213.1, found 213.0.

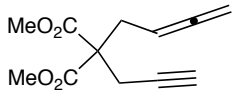


dimethyl 2-allyl-2-(buta-2,3-dien-1-yl)malonate (1.57)[27]: Sodium hydride (0.66 g of a 60% dispersion in mineral oil, 16.5 mmol) was dissolved in THF (70 mL) and cooled to 0 °C. Then, dimethyl-2-allylmalonate[32] **1.56** (2.37 g, 17.6 mmol) was added slowly via syringe. After stirring for 30 min a solution of 4-bromobuta-1,2-diene[26] **1.55** in THF was added and the reaction mixture was stirred overnight at room temperature. A saturated solution of NH_4Cl was added, and the mixture was extracted with three portions of diethylether. The combined organic phases were washed with brine, dried over

$MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (5%-8% ethyl acetate in hexanes) to afford a clear oil (1.68 g, 7.32 mmol, 55%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.57 (m, 1 H), 5.16 (app d, *J* = 5.04 Hz, 1 H), 5.12 (s, 1 H), 4.97 (m, 1H), 4.70 (dt, *J* = 2.53, 6.71 Hz, 2 H), 3.75 (s, 6 H), 2.71 (dt, *J* = 1.18, 7.48 Hz, 2 H), 2.63 (dt, *J* =2.43, 8.00 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.1, 171.0, 132.2, 119.4, 84.1, 74.6, 57.8, 52.4, 36.8, 31.8; MS (ESI) calcd for $C_{12}H_{16}O_4$ (M + Li) 231.1249, found 231.1255.

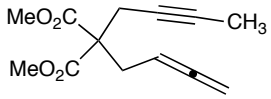


dimethyl 2-(prop-2-yn-1-yl)malonate (1.60):[33] Sodium hydride (2.9 g of a 60% dispersion in mineral oil, 72.8 mmol) was dissolved in THF and cooled to 0 °C. Then, dimethyl malonate (7.86 mL, 69.3 mmol) was added slowly via syringe. After stirring for 30 min, propargyl bromide (8.5 mL, 76.2 mmol) was added and the reaction mixture was refluxed overnight. A saturated solution of NH_4Cl was added, and the mixture was extracted with three portions of ethyl acetate. The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (4%-8% ethyl acetate in hexanes) to afford a clear oil (3.06 g, 18.0 mmol, 26 %). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.81 (s, 6 H), 3.56 (t, *J* = 7.69 Hz, 1 H), 2.83 (app dd, *J* = 2.67, 7.82 Hz, 2 H), 2.06 (t, *J* = 2.67 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2, 78.9, 70.5, 52.9, 50.8, 18.5; MS (ESI) calcd for $C_8H_{10}O_4$ (M+Li) 177.0739 found 177.0751.

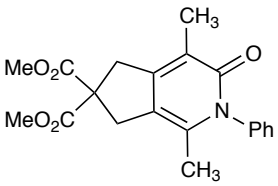


dimethyl 2-(buta-2,3-dien-1-yl)-2-(prop-2-yn-1-yl)malonate (1.61)[34]**:** Sodium hydride (0.16 g of a 60% dispersion in mineral oil, 4.1 mmol) was dissolved in THF (15 mL) and cooled to 0 °C. Then, dimethyl 2-(prop-2-yn-1-yl)malonate **1.61**[33] (0.57 g, 3.4 mmol) was added slowly via syringe. After stirring for 30 min a solution of 4-bromobuta-1,2-diene[26] **1.55** (0.5 g, 3.6 mmol) in THF was added and the white suspension was

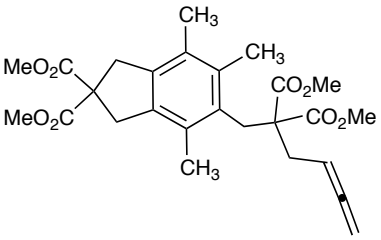
stirred for 3 h. at room temperature. After this time, the mixture was poured into a saturated solution of NH_4Cl, and extracted with three portions of ethyl acetate. The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (25% ethyl acetate in hexanes) to afford a clear oil (0.71 g, 3.19 mmol, 94%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.04-4.93 (m, 1 H), 4.72 (dt, *J* = 2.37, 6.69 Hz, 2 H), 3.78 (s, 6 H), 2.89 (d, *J* = 2.74 Hz, 2 H), 2.81 (dt, *J* = 2.31, 7.96 Hz, 2 H), 2.05 (t, *J* = 2.74 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.4, 170.2, 83.9, 78.9, 75.0, 71.7, 57.4, 53.0, 31.8, 22.9; MS (ESI) calcd for $C_{12}H_{14}NO_4$ (M+Li) 229.1052 found 220.1054.



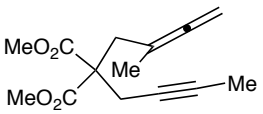
dimethyl 2-(but-2-yn-1-yl)-2-(buta-2,3-dien-1-yl)malonate (1.65)[35]: Sodium hydride (0.15 g of a 60% dispersion in mineral oil, 3.7 mmol) was dissolved in THF (30 mL) and cooled to 0 °C. Then, dimethyl 2-(but-2-yn-1-yl)malonate[36] **1.64** (0.58 g, 3.1 mmol) was added slowly via syringe. After stirring for 30 min a solution of 4-bromobuta-1,2-diene[26] **1.55** (0.46 g, 3.4 mmol) in THF was added and the suspension was stirred for 3 h. at room temperature. After this time, the mixture was poured into a saturated solution of NH_4Cl, and extracted with three portions of ethyl acetate. The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (15% ethyl acetate in hexanes) to afford a clear oil (0.71g, 3.00 mmol, 95%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.97 (m, 1H), 4.67 (m, 2 H), 3.7 (s, 6H), 2.80-2.73 (m, 4H), 1.75 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.3, 170.6, 100.2, 84.1, 74.8, 73.3, 57.7, 52.9, 31.9, 23.2, 3.7.



dimethyl-1,4-dimethyl-3-oxo-2-phenyl-5,7-dihydro-2*H*-cyclopenta[*c*]pyridine-6,6(3*H*)-dicarboxylate (1.67)[10]: The catalyst, $[Rh(COD)_2]BF_4$ (8.5 mg, 0.021 mmol) and BINAP (13.0 mg, 0.021 mmol), were added to a 2-dram vial with a teflon cap inside a nitrogen drybox. Then, outside the drybox, degassed dry toluene (4 mL) was added by syringe. Allene **1.65** (100 mg, 0.42 mmol) and phenyl isocyanate (91 μL, 0.84 mmol) were sequentially added to the reaction mixture, which was stirred for 2 days. The solvent was removed under reduced pressure and the residue was purified by column chromatography (15% ethyl acetate in hexanes) to afford compound **1.67** as a clear oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.51-7.43 (m, 4 H), 7.16 (m, 2H), 3.82 (s, 6 H), 3.50 (s, 2 H), 3.42 (s, 2H), 2.09 (s, 3H), 1.81 (s, 3H); IR (thin film) 1733.8, 1669.6, 1616.5, 1566.2 cm^{-1}; MS (ESI) calcd for $C_{20}H_{21}NO_5$ (M+H) 356.1498 found 356.1515.

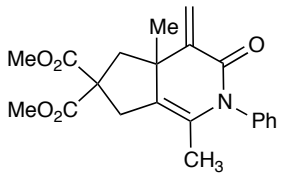


A fraction obtained from the column chromatography was identified as the homo-coupled product of **1.65.** MS (ESI) calcd for $C_{26}H_{32}O_8$ (M+H) 473.2175 found 473.2131.

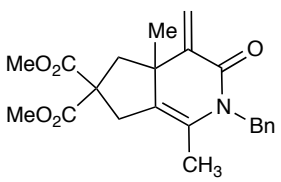


dimethyl-2-(but-2-yn-1-yl)-2-(2-methylbuta-2,3-dien-1-yl)malonate (1.70): Sodium hydride (104 mg of a 60% dispersion in mineral oil, 1.03 mmol) was dissolved in THF (15 mL) and cooled to 0 °C. Then, dimethyl 2-(but-2-yn-1-yl)malonate **1.64**[36] (0.36 g, 1.99 mmol) was added slowly via syringe. After stirring for 15 min, 4-bromo-3-methylbuta-1,2-diene **1.69**[29] (0.32 g, 2.19 mmol) was added slowly, The mixture was stirred for 2 h at room temperature. After this time, the mixture was poured into a saturated solution of NH_4Cl, and extracted with three portions of ethyl acetate. The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The

residue was obtained as a clear oil (300 mg, 1.19 mmol, 60%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.58 (m, 2H), 3.72 (s, 6 H), 2.87 (q, *J* = 2.61 Hz, 2 H), 2.75 (t, *J* = 2.55 Hz, 2 H), 1.76 (t, *J* = 2.62 Hz, 3 H), 1.70 (t, *J* = 3.21 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207. 3, 170.7, 93.5, 79.2, 75.0, 73.8, 57.3, 52.8, 35.2, 23.1, 20.6, 3.7; IR (thin film) 2212.3, 1960.1, 1733.8, 1434.4, 1194.7 cm^{-1}; MS (ESI) calcd for $C_{14}H_{18}O_4$ (M+Li) 257.1365 found 257.1307.



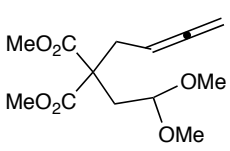
dimethyl-1,4a-dimethyl-4-methylene-3-oxo-2-phenyl-3,4,4a,5-tetrahydro-2H-cyclopenta[c]pyridine-6,6(7H)-dicarboxylate (1.71a): The catalyst, $[Rh(COD)_2]BF_4$ (812 mg, 0.03 mmol) and BINAP (18.0 mg, 0.03 mmol), were added to a 2-dram vial with a teflon cap inside a nitrogen drybox. Then, outside the drybox, degassed dry 1,2-dichloroethane (30 mL) was added by syringe. Allene **1.70** (120 mg, 0.6 mmol) and phenyl isocyanate (130 μL, 1.2 mmol) were sequentially added to the reaction mixture, which was stirred under reflux for 16 hours. The solvent was removed under reduced pressure and the residue was purified by column chromatography (5-20% ethyl acetate in hexanes) to afford the title compound (50 mg, 0.13 mmol, 26 %). MS (ESI) calcd for $C_{21}H_{23}NO_5$ (M+Li) 376.1736 found 376.1762. Homo-coupled product observed by mass spectroscopy. MS (ESI) calcd for $C_{28}H_{36}O_8$ (M+Li) 507.2570 found 507.2654.



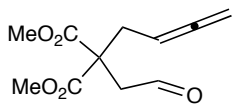
dimethyl 2-benzyl-1,4a-dimethyl-4-methylene-3-oxo-3,4,4a,5-tetrahydro-2*H*-cyclopenta[*c*]pyridine-6,6(7*H*)-dicarboxylate (171b): Following the procedure described for **1.71a**, using

benzylisocyanate ^{1}H NMR ($CDCl_3$, 300 MHz): = δ 7.51-7.15 (m, 5 H, H_{Ar}), 4.83 (s, 2H, C=CH_2), 4.27 (s, 2H, CH_2Ph), 3.66 (s, 6 H, OCH_3), 2.93 (s, 2H, CH_2), 2.68 (s, 2H, CH_2), 1.90 (s, 3H, CH_3), 1.76 (s, 3 H, CH_3).

MS (ESI+): *m/z* $[M + H]^+$ calcd for $C_{22}H_{25}NO_5$: 384.1811; found: 384.1859.



4-dimethyl 2-(buta-2,3-dien-1-yl)-2-(2,2-dimethoxyethyl)malonate 1.75: Sodium hydride (290 mg of a 60% dispersion in mineral oil, 7.25 mmol) was mixed with THF (25 mL) and cooled to 0 °C. Then, dimethyl 2- (2,2-dimethoxyethyl)malonate[30] **1.45** (960 mg, 5.8 mmol) was added slowly via syringe. After stirring for 15 min, 4-bromobuta-1,2-diene[26] **1.55** (784 mg, 5.9 mmol) was added slowly, The mixture was stirred for 2 h at room temperature. After this time, the mixture was poured into a saturated solution of NH_4Cl, and extracted with three portions of ethyl acetate. The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (5-8% ethyl acetate in hexanes) to afford the desired compound as a clear oil (1.04 g, 3.82 mmol, 65%)**.** ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.88-4.99 (m, 1 H), 4.68 (dt, *J* = 2.39, 6.62 Hz, 2 H), 4.45 (t, *J* = 5.59 Hz, 1 H), 3.72 (s, 6 H), 3.31 (s, 6H), 2.67 (dt, *J* = 2.46, 8.10 Hz, 2 H), 2.26 (d, *J* = 5.72 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.2, 171.4, 102.2, 84.4, 75.02, 55.6, 53.9, 52.7, 35.9, 33.0; IR (thin film) 2951.9, 2836.5, 1741.1, 1439.1 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{20}O_6$ (M + Li) 279.1420 found 279.1347.



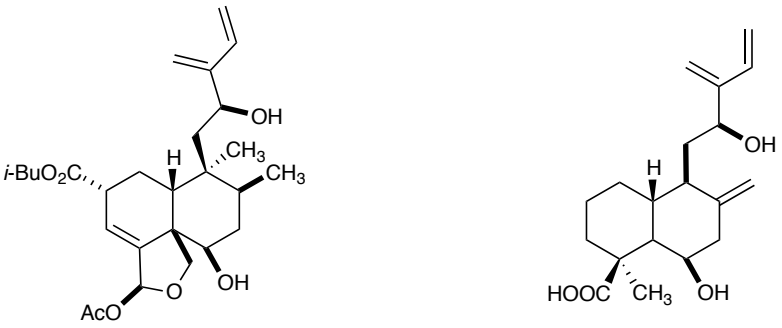
dimethyl 2-(buta-2,3-dien-1-yl)-2-(2-oxoethyl)malonate 1.76: Acetal **1.75** (104 mg, 0.38 mmol) was dissolved in acetone (15 mL) and $FeCl_3{\cdot}SiO_2$ (175 mg, 0.11 mmol) was added. The mixture was stirred for 1 h, filtrated though

florisil and washed with ethyl acetate. The solvent was removed under recurred pressure to give a clear oil (83 mg, 0.37 mmol, 99%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.73 (s, 1H), 4.97 (m, 1 H), 4.69 (dt, *J* = 2.36, 6.7 Hz, 2 H), 3.76 (s, 6H), 3.05 (s, 2H), 2.73 (dt, *J* = 2.38, 7.98 Hz, 2H).

2. CHROMIUM-CATALYZED SYNTHESIS OF (SILYLMETHYL)ALLENES AND 1,3-BUTADIENES

2.1. Introduction

1,3-butadien-2-ylcarbinols are highly functionalized molecules attractive to organic chemists due to their versatility as building blocks in organic synthesis[37] and the abundance of this motif in natural products. As an example, 1,3-butadien-2-ylcarbinol fragment is present in caseamembrol B and 12-(*S*)-hydroxylabda-8(17),13(16),14-trien-19-oic acid. (Figure 2.1) Caseamembrol shows significant cytotoxic activity against human prostate tumor cells and was isolated from extracts of *Casearia membranacea*.[37j] On the other hand, 12-(S)-hydroxylabda-8(17),13(16),14-trien-19-oic acid is a terpenoid isolated from *Thuja standishii* that shows activity as a potential cancer preventive agent.[37g]



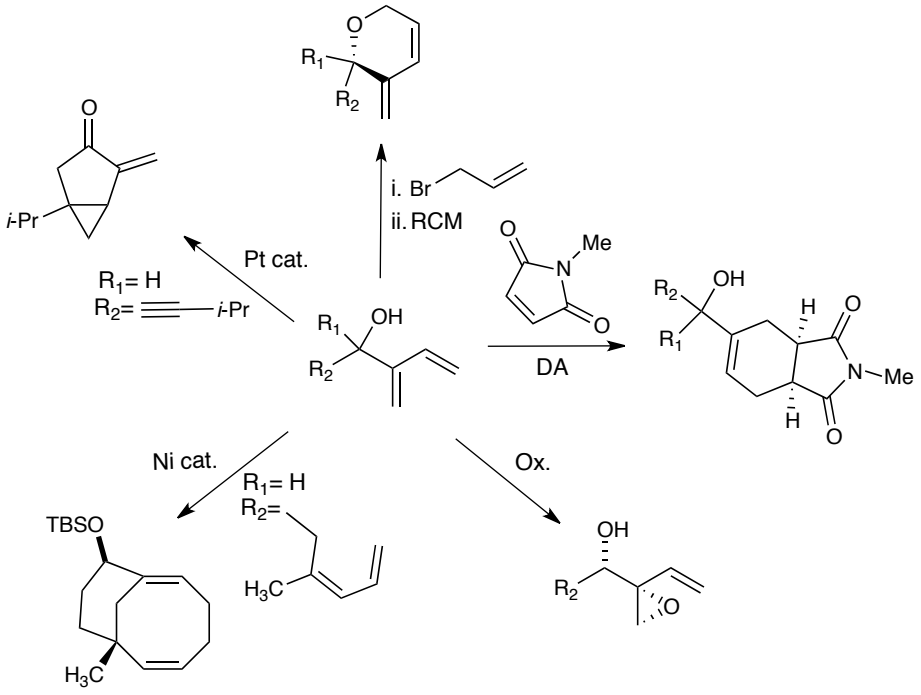
caseamembrol B **12-(*S*)-hydroxylabda-8(17),13(16),14-trien-19-oic acid**

Figure 2.1. 1,3-butadien-2-ylcarbinol fragments in natural products.

The usefulness of functionalized dienes in organic synthesis is illustrated in Scheme 2.1. Among the documented transformations of 1,3-butadien-2-ylcarbinols can be listed: Diels-Alder

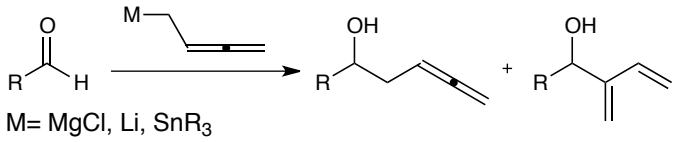
cycloadditions[37a], allylation and ring closing metathesis to afford spirocyclic compounds[38], gold[37h] and nickel[37m] catalyzed cyclizations to afford bicyclic compounds and oxidations to give vinylic epoxides.[37e]

Scheme 2.1. Reactions of 1,2-butadien-2-ylcarbinols.



A number of methodologies have been developed for the synthesis of 1,3-butadien-2-ylcarbinols. Early protocols include addition of Grignard[39] and lithium[40] reagents to aldehydes or epoxides (Scheme 2.2). The majority of these methods gave low regioselectivity, providing mixtures of 1,3-butadien-2-ylcarbinols and allenic alcohols. Therefore, methodologies involving the use of different organometallic reagents, such as tin[41], boron[42] and silicon[37d,37e] compounds, were developed to overcome regioselectivity problems and achieve modest to high enantioselectivities.

Scheme 2.2. Addition of homoallenic organometallic reagents to aldehydes.



Unfortunately, the above-mentioned procedures require the preparation of non-readily available organometallic starting materials as well as the use of considerable amounts of toxic reagents. Recently, new approaches have emerged to avoid these drawbacks. (Scheme 2.3) [37a, 38, 43] For instance, Chan *et al*. developed an indium-mediated coupling in aqueous media where the active organoindium intermediate is formed *in situ*.[43c] In more distinctive approaches, Alcaraz *et al* reported the homologation of chiral epoxy bromides while Diver and co-workers developed an alkyne-ethylene cross-methatesis protocol to provide the corresponding 1,3-butadien-2-ylcarbinols.[43a, 43b] More recently, Yamamoto *et al*. reported an enantioselective protocol which allows the formation of 1,3-butadien-2-ylcarbinols with high enantioselectivity and moderate yields by directly coupling aldehydes with 4-bromobuta-1,2-diene.[43d]

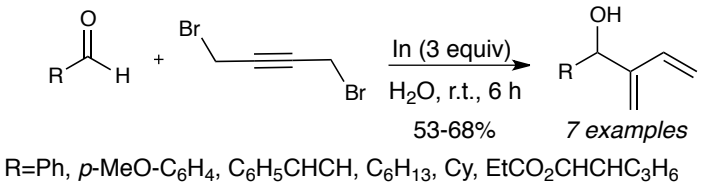
Although the methods recently developed have overcome many of the limitations presented by early approaches, only a few enantioselective synthetic procedures are known and which present various drawbacks including limited functional group tolerance or low reactivity that results in modest yields. Hence, there is an interest in developing an alternate method for the synthesis of 1,3-butadien-2-ylcarbinols.

2.2. Asymmetric synthesis of butadienylcarbinols via (silyl)allenic alcohols from chromium-catalyzed additions to aldehydes

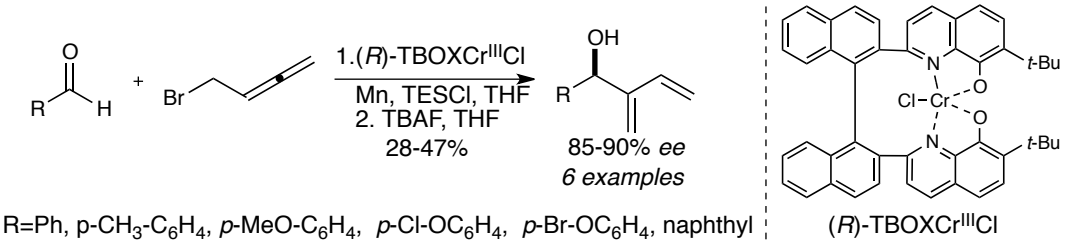
2.2.1. Background

(Allenylmethyl)silanes are powerful synthetic reagents capable of reacting with a wide variety of electrophiles to afford 1,3-dienyl-2-yl compounds.[41d, 44] It is known that (trimethylsilyl)methyl allenic alcohols provide the corresponding 1,3-butadien-2-ylcarbinols by treatment with hydrofluoric acid.[41d] Previous synthesis of (trimethylsilyl)methyl allenic alcohols have a limited substrate scope and require the use of a propargylic stannane which is prepared by a lengthy 4-step synthesis (Scheme 2.4).[41d, 45] Consequently, a novel, efficient method for the preparation of (trimethylsilyl)methyl allenic alcohols is desirable.

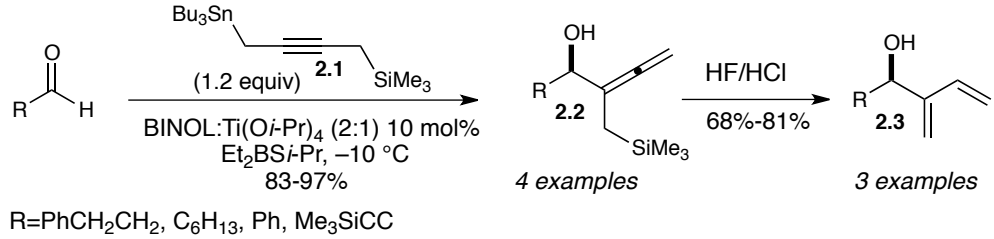
Scheme 2.3. Syntheses of 4-bromobuta-1,2-dienes.



Scheme 2.3. Continued.



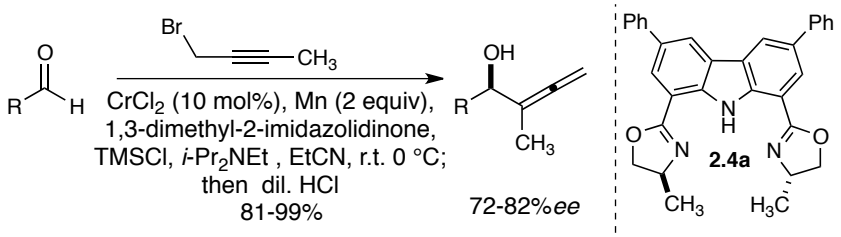
Scheme 2.4. Titanium-catalyzed synthesis of (trimethylsilyl)methyl allenic alcohols.[41d]



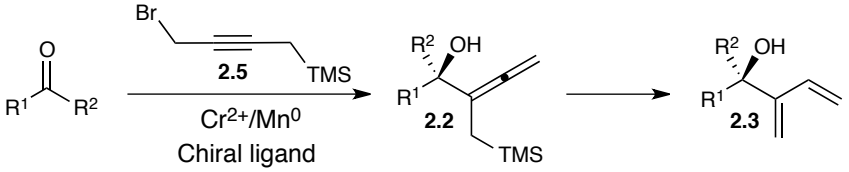
Among the synthesis for allenic alcohols, Cr/Mn redox system catalyses the enantioselective allenylation of aldehydes with propargyl bromides or 4-bromobuta-1,2-diene (Scheme 2.5).[46] The asymmetric allenylation utilizing tridentate bis(oxazoline) carbazole ligands **2.4** developed by Nakada and co-workers is among these reports. These carbazole ligands attracted our attention because they proved to be an excellent source of chirality for these asymmetric Nozaki-Hiyama-Kishi type reactions.[46c, 47]

We envisioned that the chiral (trimethylsilyl)methyl allenic alcohols **2.2** can be prepared regioselectively by the chromium catalyzed allenylation of aldehydes with (4-bromobut-2-ynyl)trimethylsilane **2.5** as a diene equivalent and utilizing the bis-oxazoline carbazole ligands **2.4** (Scheme 2.6). Herein, we describe the racemic and enantioselective synthesis of (trimethylsilyl)methyl allenic alcohols and its transformation to 1,3-butadien-2-ylcarbinols.

Scheme 2.5. Asymmetric Nozaki-Hiyama-Kishi allenylation.[46c]



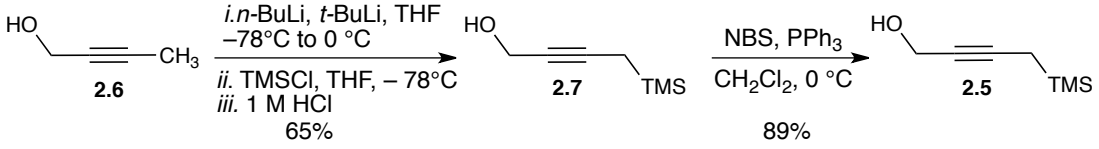
Scheme 2.6. Strategy towards 1,3-butadien-2-ylcarbinols.



2.2.2. Synthesis of butadienylcarbinols via (silyl)allenic alcohols from chromium catalyzed additions to aldehydes

Initial studies focused on the synthesis of (trimethylsilyl)methyl allenic alcohols from aldehdyes. The propargylic bromide (4-bromobut-2-ynyl) trimethylsilane **2.5** was prepared from but-2-yn-1-ol by a two step procedure (Scheme 2.7).[48]

Scheme 2.7. Synthesis of (4-bromobut-2-ynyl) trimethylsilane

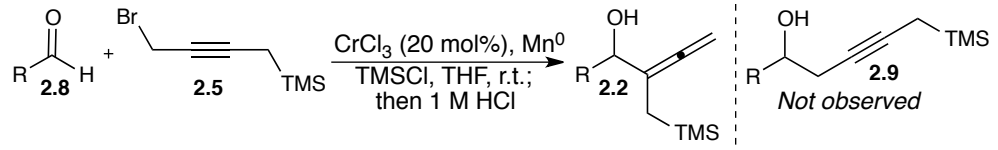


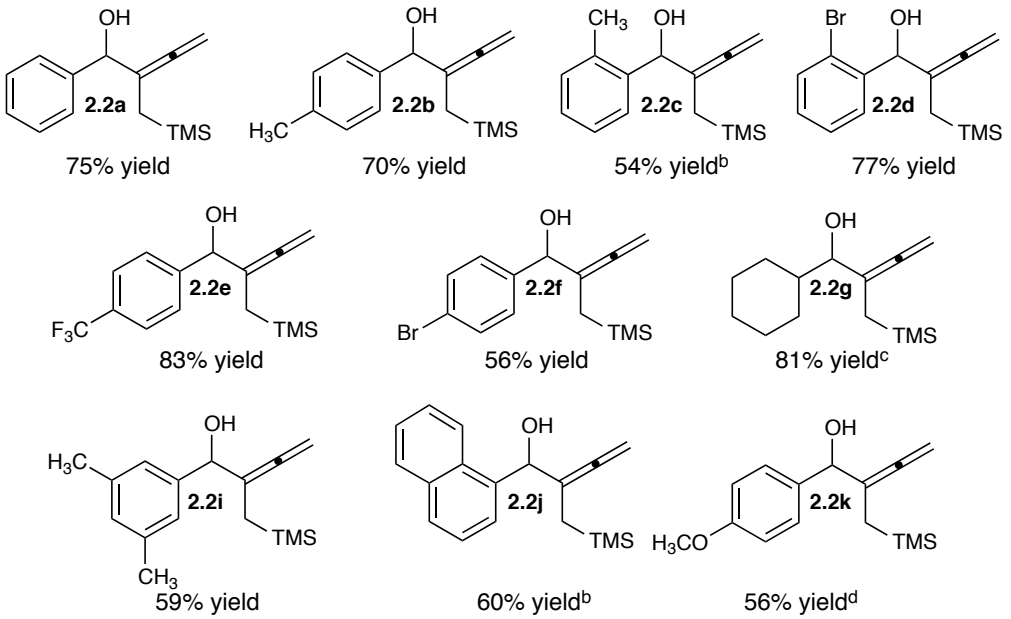
Benzaldehyde was combined with **2.5** in the presence of a catalytic amount of $CrCl_3$, 2 equiv Mn^0 and 1.1 equiv TMSCl in THF. The desired allenic alcohol **2.2a** was formed in 75%

yield after 16 h with excellent regioselectivity. More significantly, the corresponding regioisomer was not observed (Table 2.1, entry 1). To explore the scope of the reaction, various aldehydes were examined as substrates. Aromatic aldehydes containing *meta* substituents are excellent substrates for this reaction and afford the corresponding product in good yields (entry 2). However, more sterically hindered aldehydes required a longer reaction time, but the desired product was obtained in good yield after 48 h (entries 3 and 9). Allenic alcohol **2.2d** was obtained after only 16 hours despite the presence of an *o*-bromo substituent (entry 4). The formation of allenic alcohols proceeded rapidly with good yields with aromatic aldehydes containing electron-withdrawing substituents (entries 4, 5 and 6) and aliphatic aldehydes (entry 7). When *meta* substituted aldehydes are used, the product is obtained with 59% yield (entry 8). In the case of *p*-methoxybenzaldeyde only, the desired product is obtained when $CrCl_2$ is utilized for the allenylation reaction (entry 10).

A pausible mechanism for this allenylation reaction is described in Scheme 2.8. Based on the mechanism for the catalytic redox Cr(II)/Cr(III) proposed by Fürstner *et al.*,[46b] a chromium II species inserts into the C-Br bond of **2.5** forming CrX_3 and the corresponding organochromium nucleophile, which exist as a mixture of proparylic **2.10** and allenic **2.11** species. The organochromium nucleophile then reacts with the aldehyde, presumably via a 6-membered transition state, forming chromium alcoxide **2.12,** which reacts with TMSCl to liberate a second molecule of CrX_3 and form silyl ether **2.13**. Chromium (III) salts are reduced by manganese to CrX_2, which starts again the catalytic cycle. The steric properties of the substrate are one of the factors that strongly influence the equilibrium between the propargylic **2.10a** and allenylic **2.11a** chromium species (See Table 2.2).[49] The regioselectivity of this transformation can be explained by the formation of organochromium **2.10** over **2.11** avoiding unfavorable steric interactions between chromium and the silicon moiety.

Table 2.1. Scope of the chromium-catalyzed allenylation reaction.[a]





[a] Reaction conditions: (4-bromobut-2-ynyl)trimethylsilane (**2.5**) (1.1 equiv), $CrCl_3$ (20 mol%), Mn^0 (2 equiv), TMSCl (1.1 equiv), THF, 16 h; 2 mL of 1 M HCl. Isolated yields. [b] Reaction time: 48 h. [c] Reaction time: 12 h. [d] $CrCl_2$ (10 mol%).

Encouraged by these results, we directed our attention to the development of a method for the asymmetric synthesis of (trimethylsilyl)methyl allenic alcohols. For this purpose, bis(oxazoline)carbazole **2.4b** was prepared.[47b, 50] Suzuki coupling of **2.14** with phenyl boronic acid afforded carbazole **2.16b**. Then iodination, palladium-catalyzed carbonylative amidation and $BF_3{\cdot}Et_2O$ mediated cyclization afforded the corresponding carbazole. To confirm the enantiopurity**,** **2.4b** was employed in the chromium-catalyzed allylation of benzaldehyde following the known procedure (Scheme 2.9).[47b]

Scheme 2.8. Proposed mechanism for the synthesis of allenic alcohols **2.2a**.

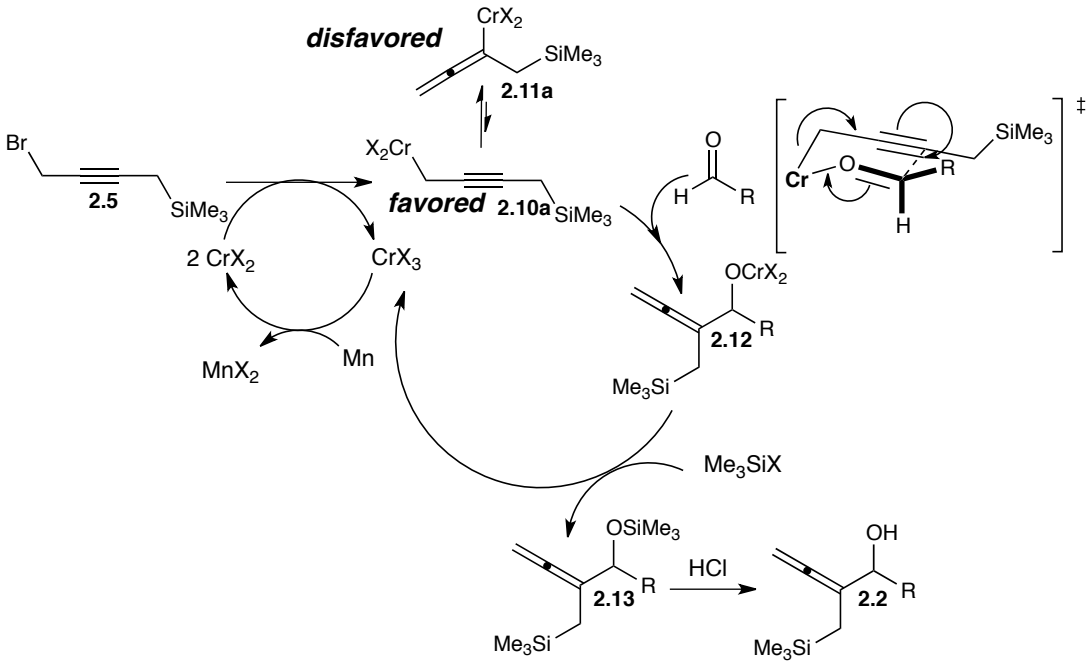
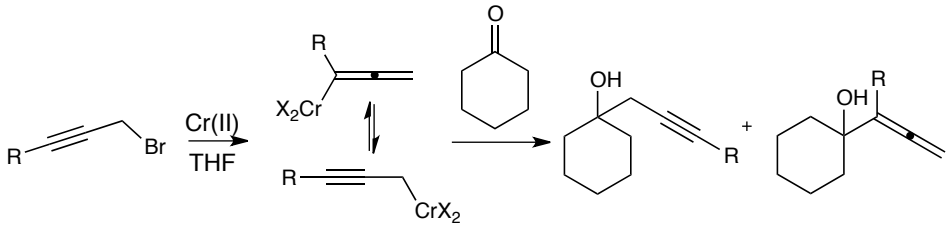
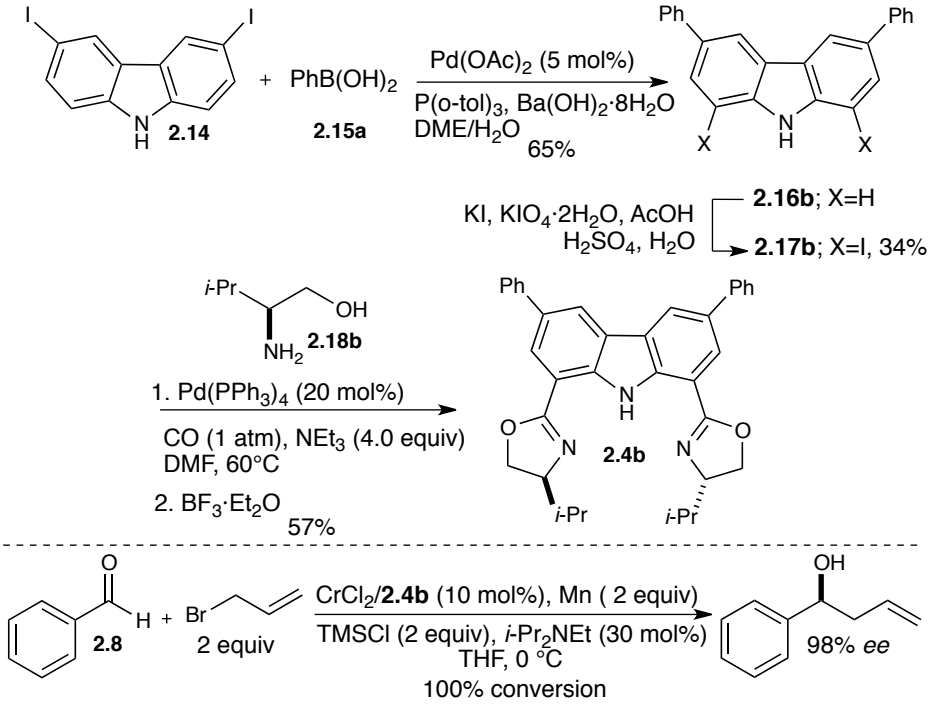


Table 2.2. Effect of propargyl bromide substitution on the regioselectivy of chromium-catalyzed allenylation.[49]



entry	R	yield (%)	acetylenic:allenic alcohols
1	H	68	65:35
2	C_5H_{11}	78	0:100
3	Ph	77	0:100
4	C_6H_{11}	75	0:100

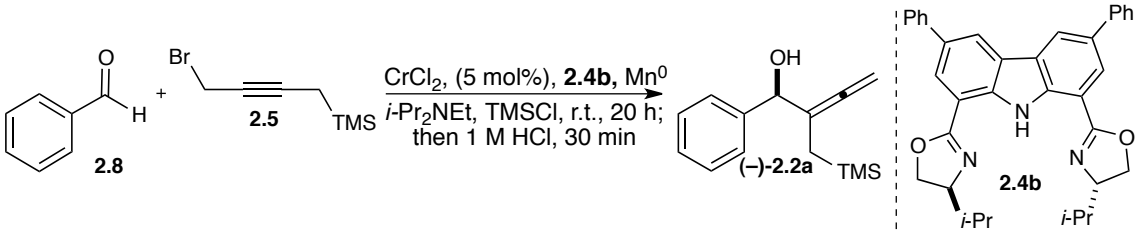
Scheme 2.9. Synthesis of bis(oxazolike)carbazole **2.4b**.[47b, 50]



When ligand **2.4b** was utilized in THF (Table 2.3, entry 1), the desired alcohol **(–)-2.2a** was obtained after 20 h in 31 % *ee*. The *ee* value increased to 46% when $CrCl_2$ was used (entry 2). To optimize the reaction conditions, different solvents were explored (entries 3 to 6). No product was observed when 1,2-dimethoxyethane was used, while DMF and EtCN[46c] afforded the desired product with poor to moderate enantiomeric excess (entries 4 and 5). MeCN became the solvent of choice, increasing the *ee* value to 73%. Next, the effect of catalyst loading was studied (entries 7 and 8). Decreasing the amount of $CrCl_2$ and ligand to 5 mol% had virtually no effect on the *ee* value (entries 6 and 7) but, when the amount was further reduced to 2.5 mol% the *%ee* decreased considerably (entry 8). A slight increase in the *%ee* value was observed with 5 mol% of the catalyst and 2 equiv Mn^0 (entry 9). Under these conditions, the starting material was completely consumed after 36 h (entry 10). Additional Mn^0 (5 equiv) reduced the *%ee*

(entry 11). When a bulkier silyl group such as DMPS was used as a substituent on the propargyl bromide, a decrease in the product yield and *%ee* was observed.

Table 2.3. Optimization of enantioselective reaction conditions.[a]

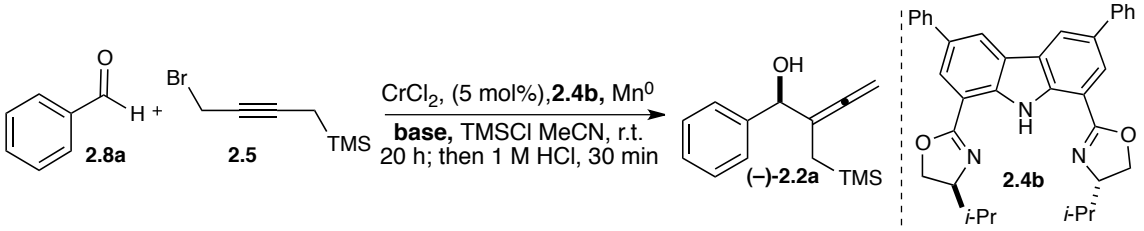


entry	$CrCl_2$(%)	Mn^0(equiv)	solvent	yield(%)	*ee*(%)[b]
1	10% $CrCl_3$	1.5	THF	99	31
2	10	1.5	THF	99	46
3	10	1.5	DME	0	0
4	10	1.5	DMF	74	8
5	10	1.5	EtCN	95	48
6	10	1.5	CH_3CN	99	73
7	5	1.5	CH_3CN	--	72
8	2.5	1.5	CH_3CN	--	51
9	5	2	CH_3CN	91	75
10[c]	5	2	CH_3CN	99	78
11	5	5	CH_3CN	--	21

[a] Reaction Conditions: (4-bromobut-2-ynyl)trimethylsilane (**2.5**) (1.5 equiv), $CrCl_2$ (5 mol%), ligand **2.4b** (5 mol%), Mn^0 (2 equiv), TMSCl (1.1 equiv), *i*-Pr_2NEt (0.3 equiv), 20 h; 2 mL of 1 M HCl. [b] Enantiomeric excess determined by chiral HPLC. [c] Reaction time: 36 h.

The reaction rate is not dependent on the base employed. On the other hand, the %ee is higher when i-Pr_2NEt, 2,6-lutidine or pyridine is used (Table 2.4, entries 1 to 3). Bases with more steric hindrance such as 2,6-di-tert-butylpyridine, DBU or DABCO decreased the %ee value (entries 5, 9, and 10).

Table 2.4. Screening of bases.[a]



entry	base	%conversion	*ee*(%)[b]
1	i-Pr_2NEt	91	78
2	2,6-lutidine	97	74
3	pyridine	99	68
4	4-*t*-Bupyridine	85	26
5	2,6-*t*-Bupyridine	99	40
6	2-chloropyridine	86	52
7	2-bromopyridine	95	52
8	1,8-bis(dimethylamino)naphthalene	99	45
9	DBU	99	29
10[c]	DABCO	98	24
11	K_2CO_3	95	11

[a] Reaction Conditions: (4-bromobut-2-ynyl)trimethylsilane **2.5** (1.5 equiv), $CrCl_2$ (5 mol%), ligand 2.4b (5 mol%), Mn^0 (2 equiv), TMSCl (1.1 equiv), i-Pr_2NEt (0.3 equiv), 20 h 2 mL of 1 M HCl. [b] Enantiomeric excess and conversion determined by chiral HPLC.

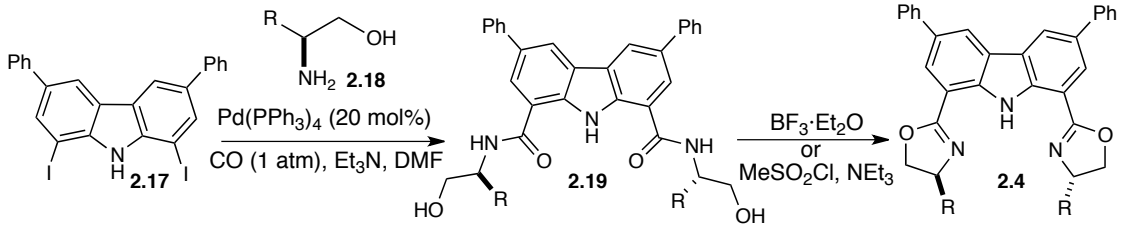
2.2.3. Synthesis of chiral bis(oxazoline)carbazole ligands

After the reaction conditions were optimized with respect to solvent, catalyst loading, Mn^0 and base, our aim was to explore the effects of carbazole ligands substitution on reaction yield and enantioselectivity. The general strategy for the synthesis of **2.4** was pictured as a coupling of di-halocarbazoles and a variety of boronic acids, followed by halogenation, carbonylative amidation and cyclization following Scheme 2.9.

First, we focused in the variation of the substituent on the oxazoline group of ligand **2.4**. For this purpose, amides **2.19** were obtained from the palladium-catalyzed carbonylative

coupling of diiodocarbazole **2.17** and different aminoalcohols, derived by reduction of the corresponding chiral amino acids. (Table 2.5) Bis-oxazoline **2.4a** was isolated in 48% yield after two steps when subjected to $MeSO_2Cl$ mediated cyclization (entry 1). As it was mentioned before, compounds **2.4b** and **2.4c** were obtained following literature procedures.[47b, 50] Bis(oxazolinyl)carabazoles **2.4d** and **2.4e** were obtained in 27% and 25% respectively (entries 4 and 5) after BF_3•OEt_2 mediated cyclization. Carbonylative amidation of **2.17** with amino alcohol **2.18f**[51] provided the corresponding amide which gave the desired ligand in 61% yield after $MeSO_2Cl$ cyclization. (entry 4).

Table 2.5. Synthesis of bis(oxazolinyl)carbazoles from **2.17**.[a]

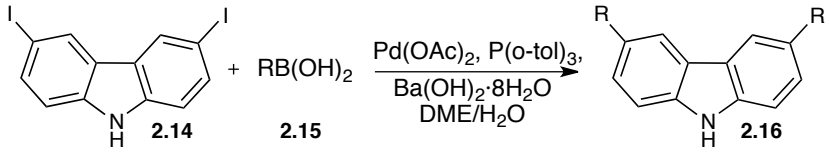


entry	R	product	yield (%)[b]
1[c]	CH_3	**2.4a**	48
2	*i*-Pr	**2.4b**	57
3	*t*-Bu	**2.4c**	4
4	Ph	**2.4d**	27
5	Bn	**2.4e**	25
6[c]	$CH(OCH_3)CH_3$	**2.4f**	61

[a] Aminoalcohol (2.5 equiv) CO (1 atm), $Pd(PPh_3)_4$ (20 mol%), NEt_3 (4.0 equiv), DMF, 60 °C, 8 h. Then BF_3•Et_2O, 120 °C, 6 h. Absolute configuration is as indicated, except for compounds **2.4d** and **2.4f**, for which the absolute configuration is (*R*). [b] Isolated yields. [c] (i) $MeSO_2Cl$ (2.5 equiv), NEt_3 (2.0 equiv), CH_2Cl_2, 0 °C to rt, 12 h. (ii) 5% alc KOH, reflux, 4 h.

Next, we turned our attention to the synthesis of ligands with different substituents in the carabazole nucleous. Thus, 3,6–disubstituted carbazoles **4.16a-c** were prepared by Suzuki coupling of 3,6-diiodo-9*H*-carbazole with the corresponding boronic acid **2.15** in the presence of $Pd(OAc)_2$ catalyst (Table 2.6). While carbazoles **2.16a** and **2.16b** were obtained with excellent yield, carbazole **2.16c** was prepared with moderate yield.

Table 2.6. Suzuki coupling of 3,6-diiodo-9*H*-carbazole with boronic acids **2.15**.[a]

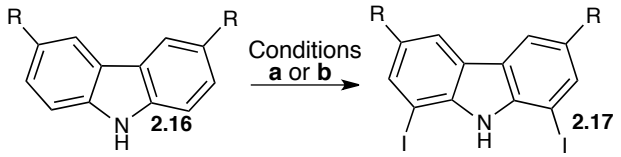


entry	R	product	yield (%)[b]
1	Ph	**2.16a**	65
2	α-naphthyl	**2.16b**	79
3	β-naphthyl	**2.16c**	23

[a] $R^1B(OH)_2$ 2.15 (3.0 equiv), $Pd(OAc)_2$ (5 mol%), P(*o*-tol)$_3$ (10 mol%), $Ba(OH)_2{\cdot}8H_2O$ (3.0 equiv), DME/H_2O, 80 °C, 8 h. [b] Isolated yields.

Substituted carbazoles **2.16** were then halogenated to complete the preparation of the carbonylative amidation substrates. (Table 2.7) Carbazole **2.16a** was prepared by the known procedure in 38% yield.[47b] Iodination of carbazole **4b** with benzyltrimethylammonium tetrachloroiodate (BTMA•ICl_2) afforded 3,6-di-α-naphtyl carbazole **5b** in 40% yield (entry 2). Finally, carbazole **2.16c** was obtained in 80% crude yield after iodination of with a KI/KIO_4 mixture. Unfortunately, the yield decreases considerably after recrystallization from toluene when the pure compound is obtained in only 18% yield (entry 3).

Table 2.7. Iodination of 3,6-disubstituted carbazoles.



entry	R	conditions	product	yield (%)[c]
1	Ph	a	**2.17a**	34
2	α-naphthyl	b	**2.17b**	40
3	β-naphthyl	a	**2.17c**	18

a) KI, KIO_4,·$2H_2O$, AcOH, H_2SO_4, H_2O, 5 h. **b**) $BnMe_3N{\cdot}ICl_2$ (2.2 equiv), AcOH, H_2SO_4, 60 °C, overnight [c] Isolated yields.

To complete the synthesis of bis(ozaxoline)carbazoles, halogenated carbazoles **2.17** were subjected to carbonylative amidation with aminoalcohol **2.18b** followed by cyclization under the corresponding reaction conditions (Table 2.8). Carbazoles **2.17a, 2.17b** and **2.17c** gave the corresponding ligands in 57%, 35% and 25% yields respectively by $BF_3{\cdot}OEt_2$ mediated cyclization. (entries 1, 2 and 3). Ligand **2.4i** was isolated 51% when $MeSO_2Cl$ was used for the dehydrative oxazoline formation (entry 4).

For the preparation of ligand **2.4g**, 1,8-dibromo-3,6-di-*tert*-butyl-9*H*-carbazole **2.17d** was prepared by the Friedel-Crafts alkylation of carbazole **2.20** and bromination following the procedure reported by Gibson *et al*. (Scheme 2.10)[52] Chiral amino alcohol **4f** was obtained in semipure form as a yellow oil in 55% by LAH reduction of (2*S*, 3*R*)-2-amino-3-methoxybutanoin acid and used without further purification.

Scheme 2.10. Synthesis of carbazole **2.17b**.[52]

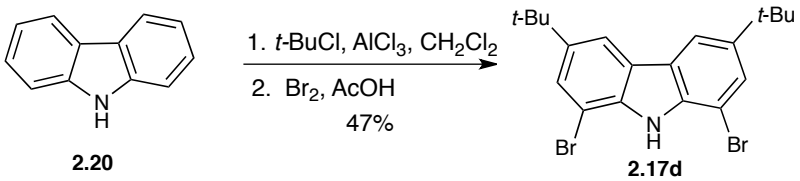
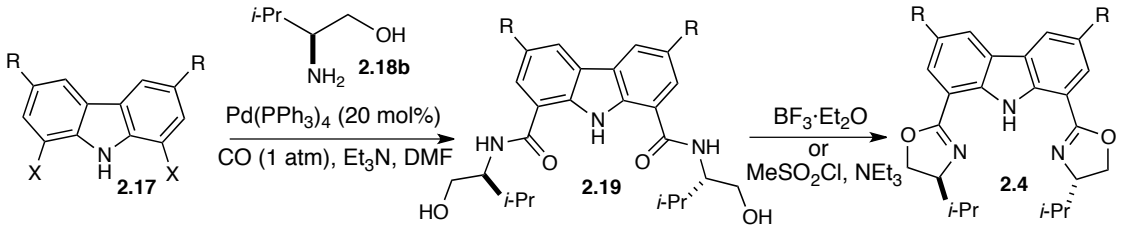


Table 2.8. Synthesis of bis(oxazolinyl)carbazoles by coupling with aminoalcohol **2.18b**.[a]



entry	R	Carbazole	X	cyclization conditions	product	yield (%)[d]
1	Ph	**2.17a**	I	b	**2.4b**	57
2	α-naphthyl	**2.17b**	I	b	**2.4g**	35
3	β-naphthyl	**2.17c**	I	b	**2.4h**	25
4	*t*-butyl	**2.17d**	Br	c	**2.4i**	51

[a] Aminoalcohol **2.18** (2.5 equiv) CO (1 atm), $Pd(PPh_3)_4$ (20 mol%), NEt_3 (4.0 equiv), DMF, 60 °C, 8 h. **b)** BF_3•Et_2O, 120 °C, 6 h **c)** (i) $MeSO_2Cl$ (2.5 equiv), NEt_3 (2.0 equiv), CH_2Cl_2, 0 °C to rt, 12 h. (ii) 5% alc KOH, reflux, 4 h. [d] Isolated yields. Dr. Worlikar is thanked for the synthesis of compounds **2.4h** and **2.4i** and their intermediates

2.2.4. Asymmetric synthesis of (silylmethyl)allenic alcohols and 1,3-butadieny-2-ylcarbinols utilizing chiral carbazole ligands

After several bis(oxazolinyl)carbazoles were synthesized, their effect in the allenylation reaction was examined. It was observed that the substituent R^1 plays an important role in the *%ee* of the reaction. Smaller R^1 substituents such as Me and *i*-Pr afforded the product with higher *%ee* values (Table 2.9, entries 1 and 2), while the bulkier *t*-Bu decreased the *%ee* value and considerably slowed the reaction rate (entry 3). Likewise, the presence of a small R^1 substituent such as a benzyl group afforded allene **(–)-2a** with higher enantiomeric excess than when a phenyl group was used (entries 4 and 5). The *%ee* of the product decreased slightly with R^1= (*R*)-1-methoxyethyl, which is not as bulky as a Ph or a *t*-Bu group (entry 6). Phenyl was the best substutient at the R^2 position, other aliphatic or aromatic R^2 substituents, including *t*-Bu, α-naphthyl and β-naphthyl, did not increase the *%ee* observed (entries 7 to 9).

Table 2.9. Effect of ligand substituent on enantiomeric excess.[a]

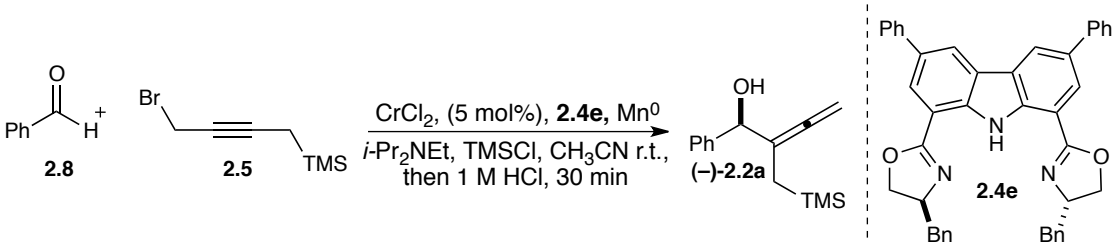
entry	ligand		%conversion	*ee*(%)[b]
1	(R^1=Me, R^2= Ph)	**2.4a**	92	74
2	(R^1=*i*-Pr, R^2= Ph)	**2.4b**	91	78
3	(R^1=*t*-Bu, R^2= Ph)	**2.4c**	86	20
4	(R^1=Ph, R^2= Ph)	**2.4d**	99	31
5	(R^1=Bn, R^2= Ph)	**2.5e**	68	75
6	(R^1= (*R*)-1-methoxyethyl, R^2=Ph)	**2.4f**	32	68
7	(R^1=*i*-Pr, R^2=α-naphthyl)	**2.4g**	99	57
8[c]	(R^1=*i*-Pr, R^2=β-naphthyl)	**2.4h**	99	21
9	(R^1=*i*-Pr, R^2=*t*-Bu)	**2.4i**	86	20

[a] Reaction Conditions: (4-bromobut-2-ynyl)trimethylsilane (**2.5**) (1.5 equiv), $CrCl_2$ (5 mol%), ligand (5 mol%), Mn^0 (2 equiv), TMSCl (1.1 equiv), *i*-Pr_2NEt (0.3 equiv), 20 h; 2 mL of 1 M HCl. [b] Enantiomeric excess and conversion determined by chiral HPLC. [c] $CrCl_2$ (3 mol%), **2.4h** (3 mol%).

Interestingly, a decrease in the reaction temperature from rt to 10 °C results in a slight decrease in the *%ee* observed from 75% *ee* to 70% *ee* (Table 2.10, entries 1 and 2). However, *%ee* was drastically reduced to 30% *ee* when the reaction temperature was further lowered to 0 °C. The same effect was observed when ligands **2.4b** or **2.4e** were utilized for the reaction. A similar effect was observed by Nakada *et al.*[53] for the chromium-catalyzed allylation of aldehydes using ligand **2.23** (Scheme 1.11). These results can be explained by a decrement on the solubility of the chiral chromium complex at low temperature, which makes the catalyst less available for the reaction while manganese reacts to give a racemic alcohol. Furthermore, when allenic alcohol **(–)-2.2a** is resubmitted to the reaction conditions at 0 °C a decrease in the *ee* value from 72% to 62% *ee* occurs. This indicates that a racemization process takes place under

the reaction conditions at low temperature. On the contrary, when **(–)-2.2a** is resubmitted to the reaction conditions at room temperature, no racemization is observed.

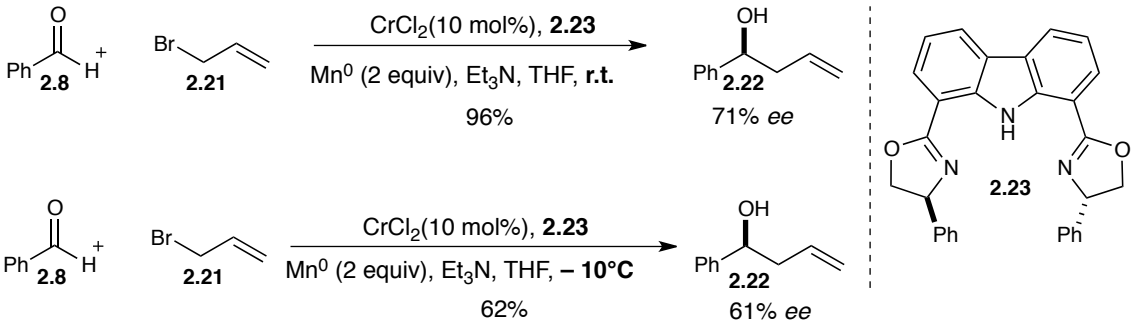
Table 2.10. Effect of temperature on enantiomeric excess.[a]



entry	Temperature (°C)	*ee*(%)[b]
1	rt	75
2	10	70
3	0	30

[a] Reaction Conditions: (4-bromobut-2-ynyl)trimethylsilane (**2.5**) (1.5 equiv), $CrCl_2$ (5 mol%), ligand **2.4e** (5 mol%), Mn^0 (2 equiv), TMSCl (1.1 equiv), *i*-Pr_2NEt (0.3 equiv), 20 h; 2 mL of 1 M HCl. [b] Enantiomeric excess determined by chiral HPLC.

Scheme. 2.11. Effect of temperature in the allylation of benzaldehyde.[53]

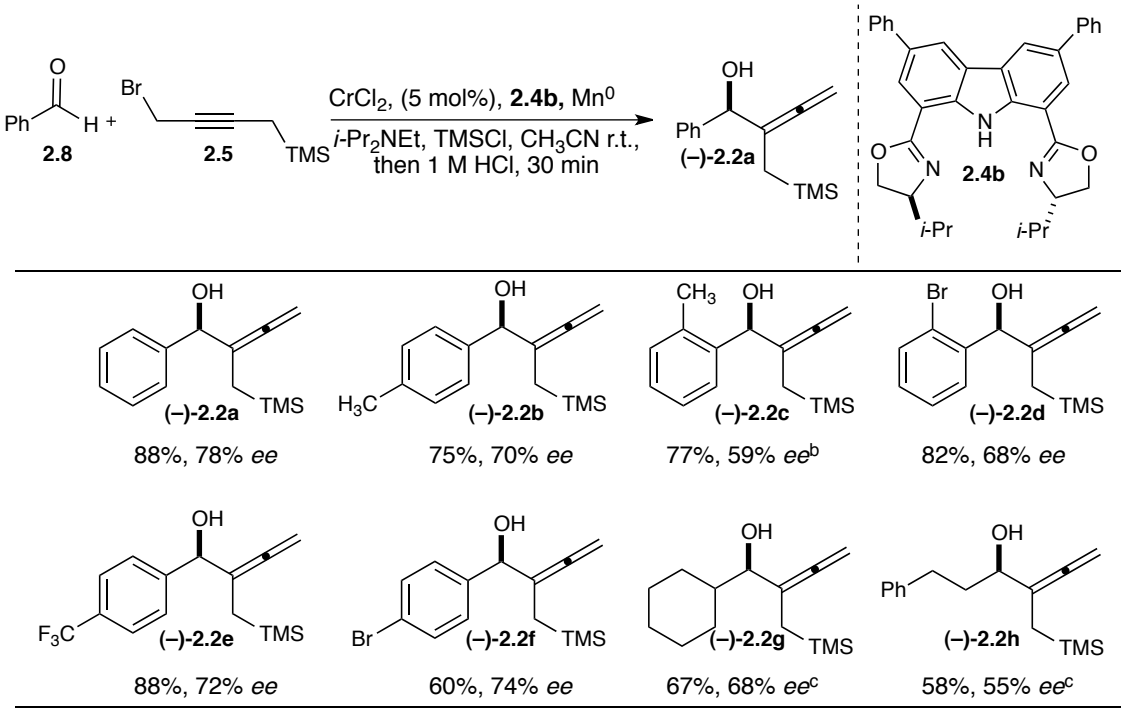


After optimizing the reaction conditions, the scope of the asymmetric reaction was examined by studying a variety of aldehydes as electrophiles (Table 2.11). *Para*-substituted or unsubstituted aromatic aldehydes are excellent substrates and afforded the desired product in high yields and good enantioselectivities (Table 2.11, compounds 1 and 2). When more sterically hindered *o*-methyl benzaldehyde was used, the reaction is slower and the enantiomeric excess dropped to 59%. Electron deficient aldehydes gave the desired product with good *ee* values (entries 4, 5, and 6). As is the case with no chiral ligands present, aliphatic aldehydes undergo reaction more quickly than aromatic aldehydes. The products derived from addition to aliphatic aldehydes afford the corresponding allenes in good yields and modest enantioselectivities. The absolute configuration of all products in Table 2.11 was established after conversion of the (trimethylsilyl)methyl allenic alcohols to the corresponding dienes and comparison of the sign of optical rotation to the known compounds.

Having the (trimethylsilyl)methyl allenic alcohols in hand, we focused on the synthesis of 1,3-butadien-2-ylcarbinols. It is known that treatment of (trimethylsilyl)methyl allenic alcohols with a mixture of hydrofluoric acid and hydrochloric acid affords the desired diene.[41d] In search of milder reaction conditions that would allow the use of this methodology in sensitive substrates, we explored the use of various fluoride sources. We found TBAF could be utilized for the clean desilylation of the (silylmethyl)allenic alcohols to afford the corresponding dienes. When **(–)-2.2a** was treated with TBAF in THF for 36 h, diene **2.3a** was obtained in 54% yield (Table 2.12, entry 1). These reaction conditions were tolerant of several functional groups and the (silylallenic)allenic alcohols synthesized were successfully transformed to 1,3-butadien-2-ylcarbinols in good to excellent yields. For most of the substrates, no regioselectivity problems were encountered and enantiopurity was retained. However, for the synthesis of compound **(–)-2.2c,** byproduct vinylsilane **2.24** was obtained, albeit in less than 5% yield (Scheme 2.12). The

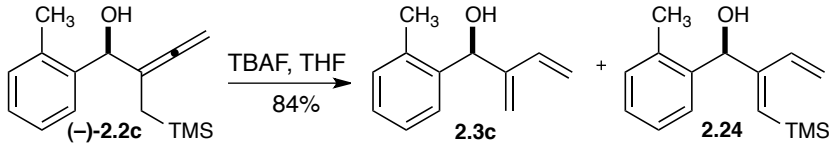
vinylsilane was also observed as a minor byproduct in the synthesis of compounds **2.3a**, **2.3b**, and **2.3d** (Table 2.12, entries 1, 2, and 4).

Table 2.11. Scope of the asymmetric chromium-catalyzed allenylation reaction.[a]



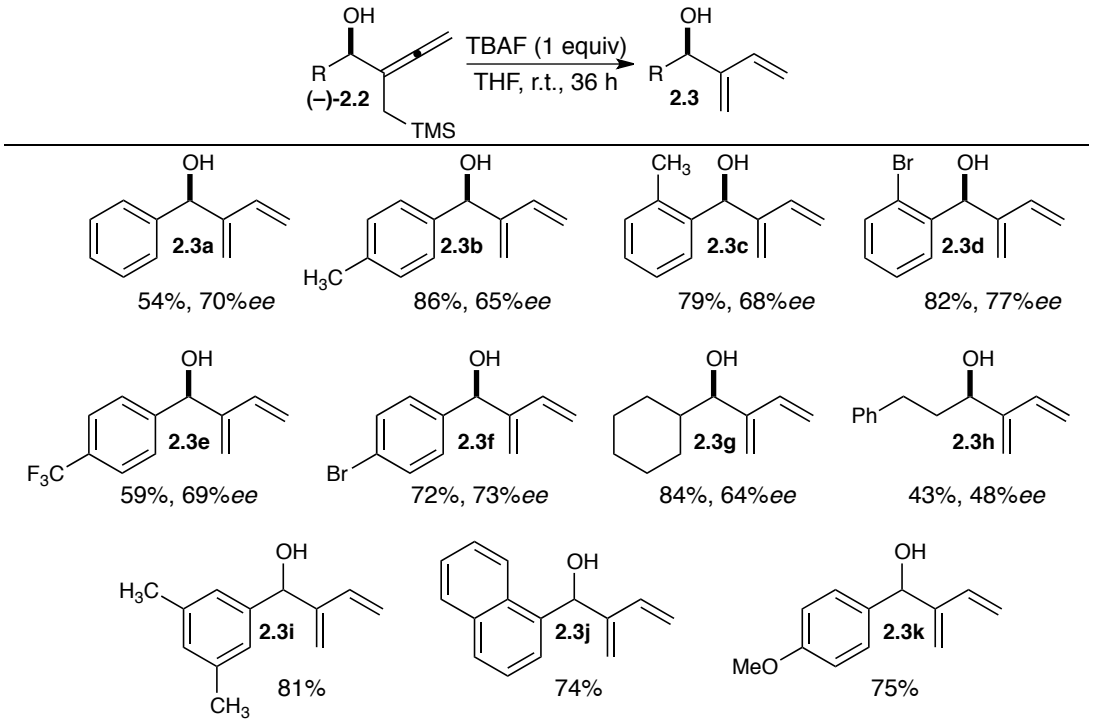
[a] Reaction Conditions: (4-bromobut-2-ynyl)trimethylsilane (**2.5**) (1.5 equiv), $CrCl_2$ (5 mol%), **2.4b** (5 mol%), Mn^0 (2 equiv), TMSCl (1.1 equiv), *i*-Pr_2NEt (0.3 equiv), 48 h; 2 mL of 1 M HCl. Isolated yields. Enantiomeric excess determined by chiral HPLC. [b] (4-bromobut-2-ynyl)trimethylsilane (3 equiv), 50 h. [c] Reaction time: 36 h.

Scheme 2.12. Synthesis of diene **2.3c**.



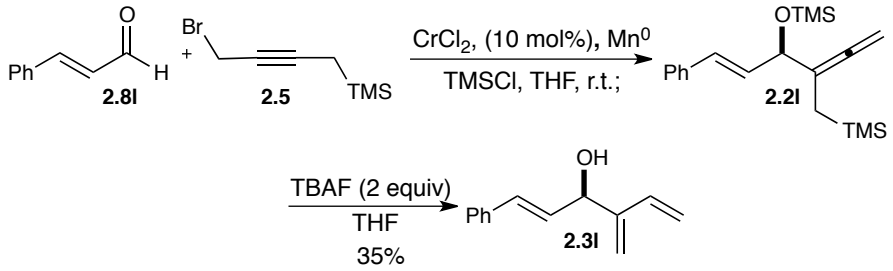
The α,β-Unsaturated aldehyde cinnamaldehyde affords TMS-protected allenic alcohols (Scheme 2.13). Bisdesilylation with TBAF in THF affords the desired adduct **2.3l** in 35% yield.

Table 2.12. Conversion of allenic alcohols to 1,3-butadien-2-ylcarbinols.[a]



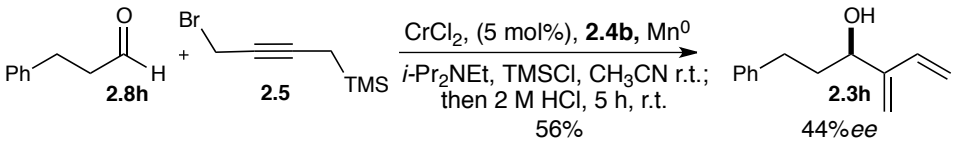
[a] Reaction Conditions: TBAF (1 equiv), THF, rt, 36 h. Isolated yields.

Scheme 2.13. Synthesis of **2.2I** from cinnamaldehyde.



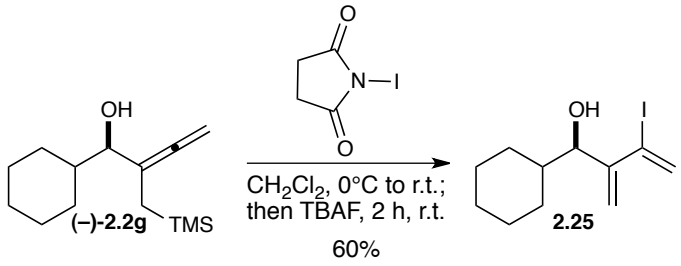
The synthesis of 1,3-butadien-2-ylcarbinols can be achieved under basic conditions but also under acidic conditions. When aliphatic allenic alcohols are treated with HCl, desilylation occurs and the corresponding dienes are obtained. The formation of 1,3-butadien-2-ylcarbinol **2.2h** from 3-phenylpropionaldehyde in one pot is illustrated in Scheme 2.14. After the aldehyde was treated with **2.5** under our reaction conditions, 2 M HCl was added to the reaction mixture and **2.3h** was obtained after 5 h in 56% yield.

Scheme 2.14. One-pot synthesis of **2.3h** from 3-phenylpropionaldehyde.



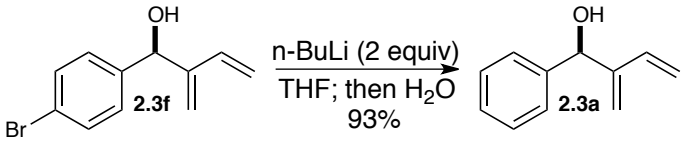
To illustrate the versatility of (trimethylsilyl)methyl allenic alcohols, **(–)-2.2g** was treated with NIS to give the iodinated adduct **2.25** in 60% yield (Scheme 2.15). During this process, the alcohol was protected *in situ* and a 1:1 mixture of the free alcohol and the silyl ether was obtained.[41d] TBAF was added after 1 h and the free alcohol **2.25** was obtained in 60% yield. The synthesis of 2-iodo-1,3-dienes can also be accomplished by treatment with I_2.[44c] Furthermore, (trimethylsilyl)methyl allenic alcohols may also be reacted with other electrophiles including Br_2[41d] and Selectfluor[44e] to afford the corresponding halogenated derivates.

Scheme 2.15. Iodination of (trimethylsilyl)methyl allenic alcohol **(–)-2.2g**.



The absolute configuration of the chiral alcohols was assigned by comparing the optical rotations of known compounds **2.3a, 2.3g** and **2.3h** with the values reported in the literature.[37d, 42a] The absolute configuration of **2.3f** was established by debromination to afford **2.3a** and comparison with the known compound (Scheme 2.16).

Scheme 2.16. Debromination of 1,3-butadien-2-ylcarbinol **2.3f**



A plausible transition state that rationalizes the observed stereochemical outcome is depicted in Figure 2.2. The propargyl moiety is in the apical, less hindered position, avoiding steric interactions with the oxazoline substituents. The aldehyde coordinates to chromium with a trans geometry and occupies the less encumbered equatorial position. Addition to the aldehyde takes place from the *Si*-face, affording the *R*-alcohol. This is comparable with the observations made by Nakada and Inoue.[46c] Nonetheless, as previously discussed,[46a, 46c] the formation of a dinuclear complex or an intermolecular mechanism cannot be ruled out at this time.[54]

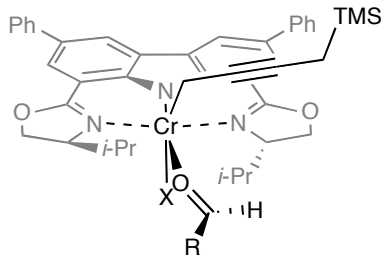


Figure 2.2. Proposed transition state for the allenylation reaction of aldehydes.

2.3. Synthesis of tertiary 1,3-butadien-2-ylcarbinols from chromium-catalyzed addition of (4-bromobut-2-ynyl)trimethylsilane to ketones

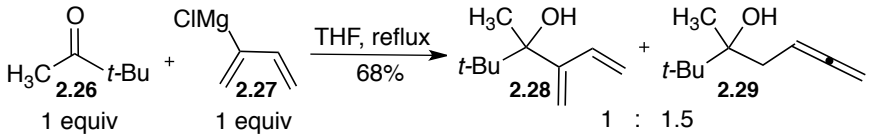
2.3.1. Introduction

Several strategies for the synthesis of 1,3-butadien-2-ylcarbinols from additions to aldehydes to afford secondary alcohols have been developed.[41a, 42a, 43c-e] However, methodologies for the synthesis of tertiary 1,3-butadien-2-ylcarbinols from ketones are scarce, regardless of their significance. Although the addition of a nucleophilic organometallic reagent to a carbonyl group is a common approach for the formation of new carbon–carbon bonds,[55] aldehydes are used for this purpose much more regularly than ketones[56], presumably due to the lower electrophilicity of ketones toward nucleophilic additions which also increases the possibility of competitive proton transfer. Among the examples of organometallic additions to ketones, the use of magnesium[39a, 39b] and lithium[40b] reagents derived from organostannanes for the synthesis of 1,3-butadien-2-ylcarbinols can be highlighted. Unfortunately, these early methods present low regioselectivity and afford mixtures of the desired diene **2.28** and the corresponding homoallenic alcohol **2.29** (Scheme 2.17).

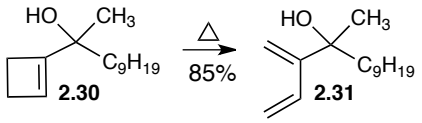
Due to this difficulty, alternative strategies have been developed. Tertiary 1,3-butadien-2-ylcarbinols can be obtained by thermal ring opening of cyclobutenyl alcohols. (Scheme 2.18)[57]

Although this method provides the desired alcohols with good yields, the required starting materials are not readily available and the substrate scope is limited. More recently, Alcaraz *et al*. reported the homologation of chiral epoxy bromides with dimethylsulfonium methylide for the synthesis of seconday and tertiary 1,3-butadien-2-ylcarbinols.[58] (See Scheme 2.3, page 38) This method provides alkyl or aryl 1,3-butadien-2-ylcarbinols with good yields. Nevertheless the substrates are not commercially available.

Scheme 2.17. Mixture of regioisomers obtained from the addition of 1,3-butadien-2-ylmagnesium chloride to 3,3-dimethylbutan-2-one [39a].



Scheme 2.18. Thermal ring opening of cyclobutenyl alcohols.[57]

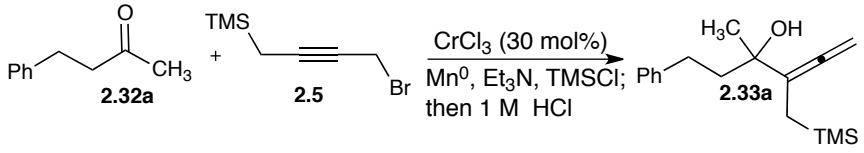


2.3.2. Results and discussion

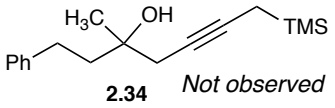
In an effort to overcome some of the drawbacks presented by the existing procedures, we aimed for the synthesis of tertiary 1,3-butadien-2-ylcarbinols utilizing the methodology described in previous sections. Even though chromium-catalyzed additions to ketones are not common,[59] it was envisioned that the allenylation of ketones and subsequent desilylation of the tertiary allenic alcohols could provide a useful approach for the regioselective synthesis tertiary 1,3-butadien-2-ylcarbinols.

The reactivity of ketones towards the chromium-catalyzed allenylation was explored. 4-phenylbutan-2-one **2.32a** was combined with 1.1 equiv of **2.5** in the presence of a catalytic amount of $CrCl_3$ and 2 equiv of Mn^0 and TMSCl in THF. After quenching with 1 M HCl the deprotected 3° allenic alcohol **2.33a** was obtained with 51% conversion (Table 2.13, entry 1). No regioisomers such as the corresponding propargylic alcohol **2.34** were observed. This is complementary to prior methods in which the formation of propargylic alcohol is favored (Scheme 2.19).[60] Increasing the equivalents of **2.5** results in an increase in conversion (entries 1 and 3) until 4 equivalents is reached, at which point a notable decrease in conversion is observed (entry 4).

Table 2.13. Optimization of the allenylation reaction.[a]

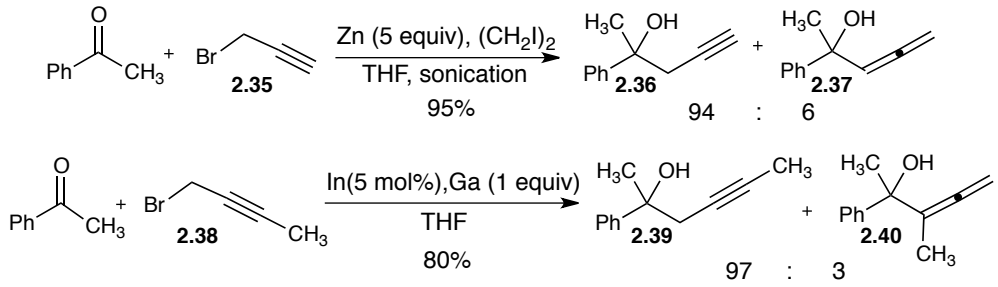


entry	TBAF (equiv)	conversion(%[b])
1	1.1	51
2	2.2	61
3	3.0	80
4	4.0	50



[a] $CrCl_3$ (30 mol%), Mn^0 (2 equiv), TMSCl (2 equiv), rt. 24h. Then 1M HCl, rt, 30 min. [b] Determined by ^1H NMR.

Scheme 2.19. Synthesis of propargylic alcohols from ketones.[60a, 60b]

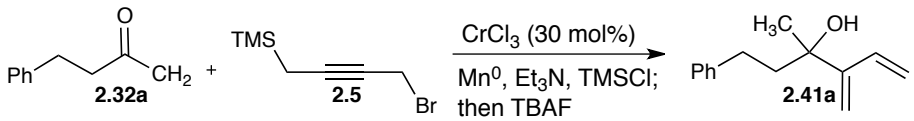


The desired 1,3-butadien-2-ylcarbinol **2.41a** was prepared *in situ* from the unpurified allene by direct treated with TBAF. Use of 2 equiv of TBAF resulted in only 25% conversion to the desired dienylalcohol (Table 2.14, entry 1). Use of excess TBAF greatly increased the product yield. The required excess can be explained by the presence of excess (4-bromobut-2-ynyl)trimethylsilane **2.5** in the reaction mixture, which competitively consumes the fluoride.

After obtaining these optimized reaction conditions for ketone addition followed by diene formation, the substrate scope was evaluated. Aliphatic methyl ketone **2.32a** is an excellent substrate for this reaction (Table 2.15). Ketone **2.32b**, which is more sterically hindered due to the presence of a secondary carbon a to the carbonyl group, is somewhat less reactive, but afforded the desired product **2.41b** in 41% yield. Cyclohexanone gave the corresponding diene **2.41c**, albeit in poor yield. Aromatic ketones including acetophenone and *p*-methylacetophenone afford the desired diene **2.41d** and **2.41e** in 45% and 53% yield, respectively. It was observed that the nature of the substituent in the aromatic group affects the rate of the reaction. Allenylation of 4-bromoacetophenone containing a slightly electron-withdrawing group in the *para* position afforded diene **2.41f** in 67% after the starting material was consumed (48 h). Reactions involving electron-rich 4-mehotoxyacetophenone did not go to completion after 48 h.

Although a 51% yield of product **2.41g** was obtained, 40% of the starting material was also recovered.

Table 2.14. Optimization of desilylation conditions.[a]

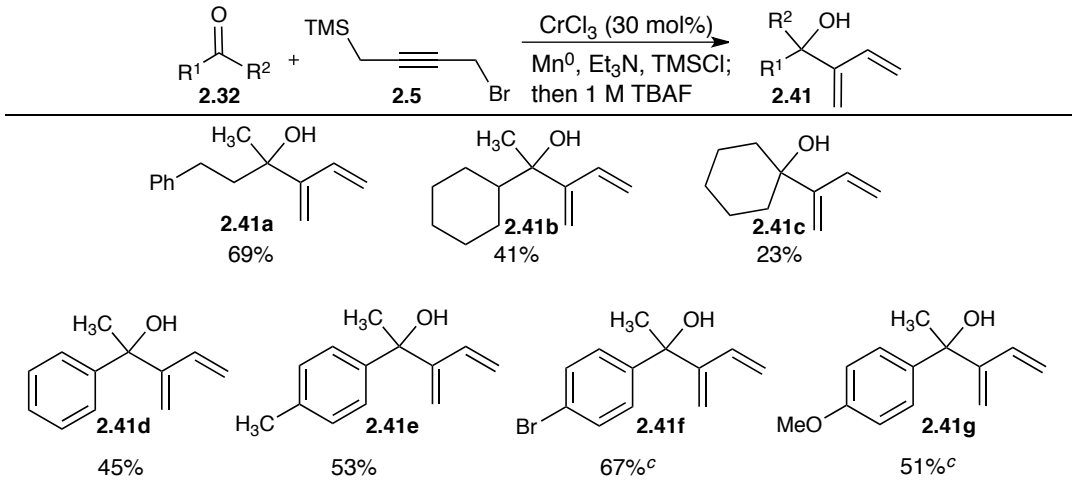


entry	TBAF (equiv)	conversion (%)[b]
1	2	25
2	3	45
3	5	68
4	8	88

[a] $CrCl_3$ (30 mol%), Mn^0 (2 equiv), Et_3N (1 equiv) TMSCl (2 equiv), rt. 24h. Then 1 M TBAF in THF, rt, 16 h. [b] Determined by ^1H NMR Spectroscopy.

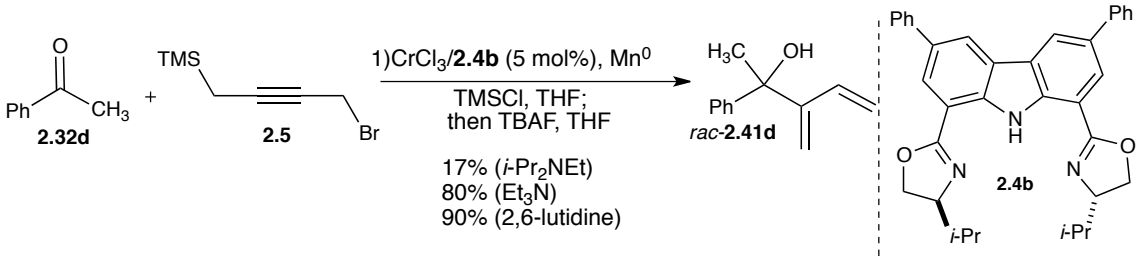
In an attempt at the asymmetric synthesis of 3° butadienylcarbinols, ketone 2.32d was submitted to the reaction conditions that we had previously developed for the enantioselective synthesis of 2° 1,3-butadien-2-ylcarbinols from aldehydes. As shown in Scheme 2.20, a racemic mixture of 2d was obtained with 17% conversion under our standard conditions. Further optimization of the reaction conditions increased the conversion to 90% when 2,6-lutidine was used as the base, when only 1.2 equiv of 2.5 were utilized. This represents a substantial increase over the yield observed in the absence of ligand (Table 15, entry 4), but no enantioselectivity was observed in the product mixture. Although this is a disappointing result on the surface, it does demonstrate that a bulky ligand does not inhibit this already hindered C–C bond forming reaction.

Table 2.15. Scope of the reaction[a].



[a] $CrCl_3$ (30 mol%), Mn^0 (2 equiv), Et_3N (1 equiv) TMSCl (2 equiv), rt. 24h. Then 1 M TBAF in THF, rt, 16 h. [b] Isolated yield. [c]Reaction time: 48 h.

Scheme 2.20. Attempted asymmetric synthesis of **2.33d**.



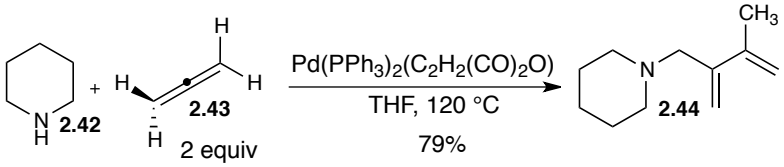
2.4. Synthesis of 2-aminomethyl-1,3-dienes from chromium-catalyzed addition of 4-bromobut-2-yn-1-yl)trimethylsilane to imines

2.4.1. Introduction and background

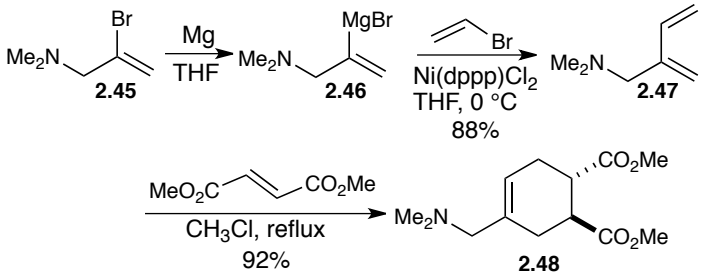
The addition of carbon nucleophiles to imines is a powerful and well-studied transformation for the preparation of nitrogen-containing organic compounds[61] and the synthesis of biologically active natural products. However, methods for the preparation of 2-

aminomethyl-1,3-dienes are still uncommon. An early report describes the palladium-catalyzed coupling of amines with 2 equivalents of propadiene to afford 2-aminomethyl-1,3-dienes. (Scheme 2.21).[62] Although the desired 1,3-dienes are obtained in moderate to good yields, the use of propadiene, a gas, is required and bis(dienyl)amines are also observed as a by-product of this palladium-catalyzed coupling. Hosomi *et al*.[63] reported the Kumada cross coupling of Grignard reagents prepared from 2-bromo-3-aminopropene to vinyl halides for the synthesis of 2-aminomethyl-1,-3dienes. This method proved to be efficient for the synthesis of the required 1,3-dienes, which were further used in Diels-Alder cycloaddition reactions (Scheme 2.22). Unfortunately, the synthesis of starting materials 2-bromo-3-aminopropene is not convenient. Although both methods afford the desired products with moderate to good yield, the substrate scope is very limited.

Scheme 2.21. Palladium coupling of allene with piperidine.[62]



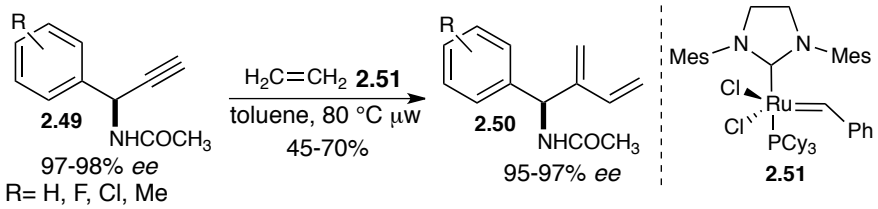
Scheme 2.22. Nickel-catalyzed synthesis of Diels-Alder reaction substrates.[63]



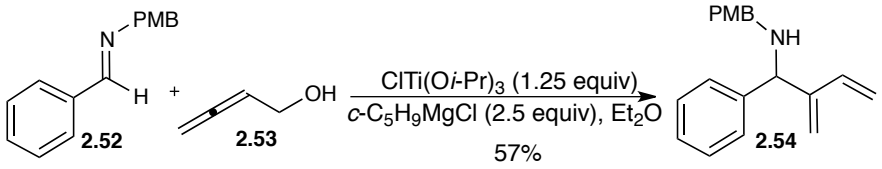
More recently, metathesis of aryl propargylic amines with ethylene, in the presence of Grubb's catalyst **2.51,** was utilized for the synthesis of 2-aminomethyl-1,3-dienes.[64] Although this method affords the desired products in moderate yields, the enantiomeric excess of the starting materials is conserved (Scheme 2.23). The adducts of interest can also be obtained by a regioselective titanium-mediated cross coupling of aryl imines with homoallenic alcohols (Scheme 2.24).[65] One of the advantages of this method is the ability to use various protecting groups on nitrogen. Unfortunately, the use of excess titanium complex is required. Finally, 2-aminomethyl-1,3-dienes were efficiently prepared by an indium mediated[66] reaction of imines with 1,4-dibromo-2-butyne **2.56** (Scheme 2.25). The scope of this method is broad and, in the presence of acid, imines can be formed *in situ* from aniline and the corresponding aldehyde to afford the desired dienes in a three-component reaction.

In view of the limited number of methods for the synthesis of 2-aminomethyl-1,3-dienes and aiming to expand the scope of the chromium-catalyzed synthesis of 1,3-butadienes described in previous sections, we decided to study the reaction of imines with (4-bromobut-2-yn-1-yl)trimethylsilane **2.5**.

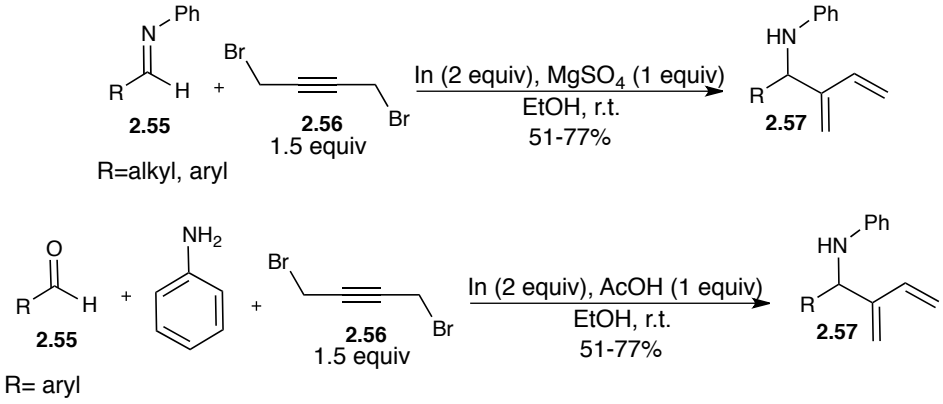
Scheme 2.23. Synthesis of 2-aminomethyl-1,3-dienes by olefin cross-methatesis. [64]



Scheme 2.24. Titanium mediated coupling of homoallenic alcohols with imines.[65]



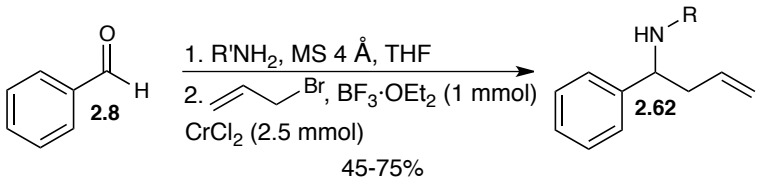
Scheme 2.25. Indium-mediated synthesis of 2-aminomethyl-1,3-dienes.[66]



2.4.2. Chromium-catalyzed allylation of imines

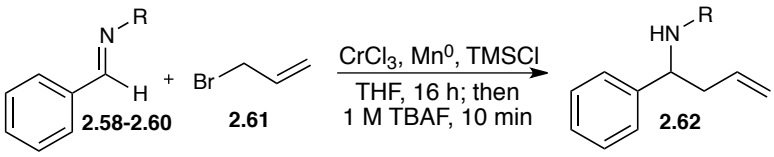
Metal-catalyzed additions to imines are well-known transformations (e.g. allylation, alkylation, propargylation, etc.)[61]. Zinc, magnesium, tin, palladium[67] and boron[68] are examples of metals used for this purpose. However, only one example of a chromium-catalyzed addition to imines has been reported (Scheme 2.26).[69] Therefore, prior to the synthesis of 2-aminomethyl-1,3-dienes, we decided to use allyl bromide for a chromium-catalyzed synthesis of allylic imines.

Scheme 2.26. *In situ* formation of imines followed by $CrCl_2/BF_3{\cdot}OEt_2$ mediated allylation.[69]



When *N*-phenyl and *N*-benzyl imines were combined with allyl bromide in the presence of a catalytic amount of $CrCl_3$, 2 equiv of Mn^0 and TMSCl, the desired product was not observed, albeit the imines were consumed as indicated by TLC (Table 2.16, entries 1 and 2). On the contrary, when *N*-tosyl imine **2.60** was used, the desired product **2.62** was obtained in 80% conversion. It was suspected that the product from the allylation of imines **2.58** and **2.59** was being formed but may be coordinating to the chromium salts present in the reaction mixture. If this were the case, the product would be lost after filtration of the reaction mixture though silica. In order to recover the desired adducts **2.62**, an excess of Et_3N and DMF was added to the mixture prior to filtration, expecting the amines will coordinate to the chromium salts releasing the desired product. (entries 4 to 6). After the products were successfully recovered, it was observed that tosyl imine, activated by the presence of an electron-withdrawing group, afforded the corresponding adduct in higher yield than N-benzyl and N-phenyl imines (entry 7).

Table 2.16. Chromium-catalyzed allylation of imines.[a]



entry	R	additive[b]	yield (%)[c]
1	Ph	--	--
2	Bn	--	--
3	Ts	--	80
4	Ph	DMF	46
5	Bn	DMF	36
6	Bn	Et_3N	38
7	Ts	Et_3N	88[d]

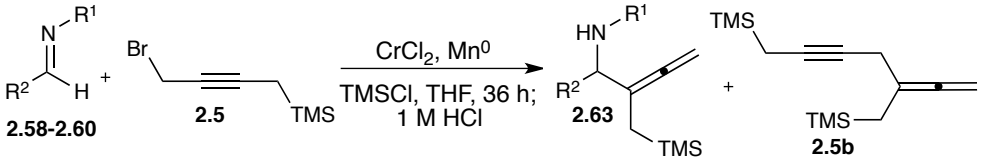
[a]Imine (1 equiv), allyl bromide (1.5 equiv), $CrCl_3$ (10 mol%), Mn (2 equiv), TMSCl (1.1 equiv), 16 h. [b] Added after 16 h; then TBAF(1 M in THF, 1 equiv). [c] Yield calculated by ^1H NMR spectroscopy. [d] Isoated yield.

2.4.3. Synthesis of (silylmethyl)allenic amines and 2-aminomethyl-1,3-dienes

Encouraged by the results obtained with the allylation of imines, we directed our attention to the synthesis of (silylmethyl)allenic amines. After imines **2.59-2.60** were submitted to our reaction conditions. The corresponding imines were mixed with (4-bromobut-2-yn-1-yl)trimethylsilane in the presence of $CrCl_2$ (10 mol%), manganese (2 equiv) and TMSCl. After 36 hours it was observed a considerable decrement on the reactivity of imines **2.58a** and **2.59** with respect to the allylation reaction (Table 2.17, entries 1 to 3). Only traces of product were observed when *N*-(4-(trifluoromethyl)benzylidene)aniline **2.58b** was used. Albeit the presence of an electron withdrawing group in the substrate, the reactivity of imine **2.58b** towards the allenylation reaction was poor. On the other hand, when activated tosyl imine **2.60** was used, the allenylated adduct was obtained in 64% conversion. Thus, confirming the presence of an electron withdrawing tosyl group is necessary to increase the electrophilicity of the substrate.

The percent conversion of the reaction did not improve when the temperature of the reaction was increased to 60°C. The homo-coupled product of (4-bromobut-2-yn-1-yl)trimethylsilane **2.5b** was observed when unreactive substrates **2.58-2.59** were used; addition of excess propargyl bromide **2.5** after 12 h did not improve the conversion of this reaction.

Table 2.17. Allenylation of imines.[a]



entry	R^1	R^2		conversion[b] (%)
1	Ph	Ph	**2.58a**	10
2	Ph	4-$CF_3C_6H_4$	**2.58b**	--
3	Bn	Ph	**2.59**	8
4	Ts	Ph	**2.60**	64

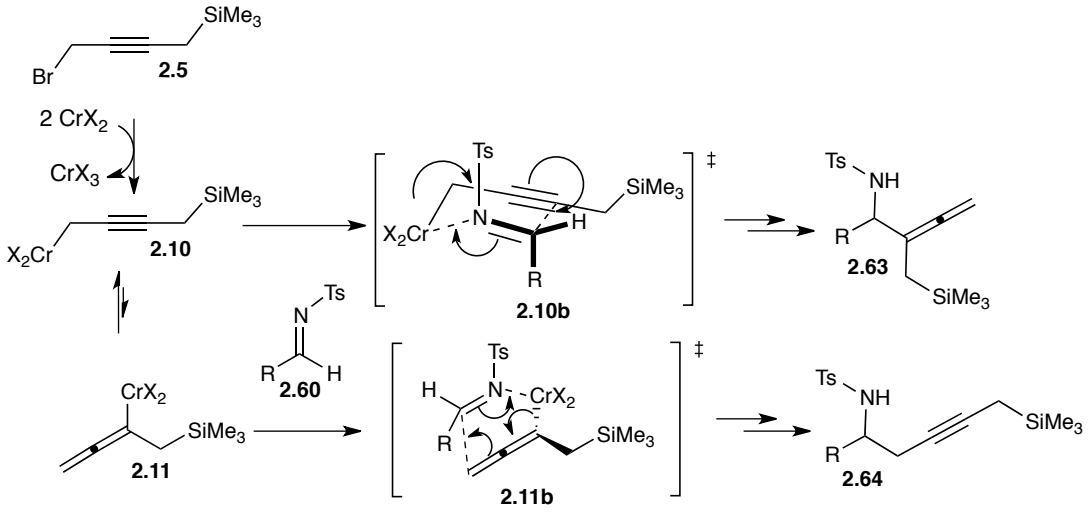
[a] Imine (1 equiv), propargyl bromide **2.5** (1.5 equiv), $CrCl_2$ (10 mol%), Mn (2 equiv), TMSCl (1.1 equiv), 36 h; then 1 M HCl (2 mL) [b] Determined by H^1 NMR spectroscopy.

Interestingly, a by-product from the reaction of tosyl imine **2.60** and propargyl bromide **2.5** was identified as the corresponding propargyl amine **2.64**. The mixture of regioisomers was observed in a 2.5:1 ratio. It is known that propargylic organometallic reagents exist as an equilibrium mixture of allenic and propargylic species[70]. Hence, the use of metal-catalyzed additions of propargylic reagents to electrophiles for the synthesis of allenic compounds has been previously limited by low regioselectivity. A regioisomeric mixture was not observed previously for the allenylation of aldehydes or ketones.

The allenylation of aldehydes with (4-bromobut-2-yn-1-yl)trimethylsilane described in section 2.22 is a highly regioselective transformation due to the preferred formation of

propargylic chromium species **2.10** over allenic intermediate **2.11**. It has been observed that not only the propargyl halide, but also the electrophile present in the reaction affects the products ratio.[49] For the synthesis of (silylmethyl)allenic amines **2.63**, the presence of a bulky N-tosyl group on the substrate should be considered. As shown in Scheme 2.27, the attack of the preferred propargylic chromium species **2.10** to tosyl imine **2.60** results in a 6-membered chair-like transition state **2.10b** with unfavorable steric interactions between chromium and the tosyl group. On the contrary, reaction of allenic chromium **2.11** with tosyl imine occurs *via* transition state **2.11b**, in which the corresponding steric interactions are minimized. Thus, resulting in the rapid formation of **2.64** even thought **2.11** is present as the minor organchromium regioisomer.

Scheme 2.27. Proposed transition states leading to the formation of regioisomers **2.63** and **2.64**.



To explain the product ratio in the context of the Curtin-Hammett principle, the reaction diagram for the allenylation reaction is depicted in Figure 3. The energy for the equilibration between organochromium species **2.10** and **2.11** ($\Delta G_{2.10-2.11}$) is greater than the activation energy

for the formation of the products ($\Delta G_{2.10-2.11} > \Delta G_{2.10-2.63}$ and $\Delta G_{2.11-2.64}$). The nucleophilic attack to the electrophile (imine or aldehyde) occurs faster than the interconvertion of the organometallic species thus the formation of allenes **2.64** and **2.2** from the attack of the more abundant chromium intermediate is favored. However, the products ratio is not only a reflection of the relative concentration of **2.10** and **2.11**. Considering transition states **2.10b** and **2.11b** for the allenylatin of tosylimine, the first is higher in energy due to the presence of unfavorable steric interactions resulting is a slower formation of **2.63** with respect to **2.64**. As a consequence of these two variables, a regioisomeric mixture is obtained where allene **2.63** is the major product. In the case for the chromium-catalyzed allenylation of aldehydes, the desired allenes **2.2** are obtained as a single product. For this transformation it can be assume that, in the absence of a bulky tosyl group, the activation energy for the allenylation of aldehydes (shown in blue) is lower or equal in energy than for the formation of the propargylic amine **2.9.** Thus, the formation of allene **2.2** is favored by both the abundance of organochorium **2.10** and a small $\Delta G_{2.10\text{-}2.2}$.

Aiming for an increment in the formation of the desired allene, the reaction conditions were optimized as described in Table 2.18. It was observed that increasing the amount of chromium catalyst accelerates the reaction rate and favors the formation of the desired allene **2.63** (entries 1 to 4). However, if the catalyst is present in 30 or 50 mol% the regioisomer ratio does not change (entry 5). When the reaction is cooled to 0 °C, alkyne **2.64** is obtained as a single product albeit in low conversion (entry 6). Increasing the reaction temperature does not increment the formation of the corresponding allene (entry 7). A large excess of propargyl bromide reduces the reaction time to 16h yet affords a 1:1.6 mixture of regioisomers (entry 10). It was also observed that using $CrCl_3$ or increasing the equivalents of TMSCl have no effect on the regioisomer ratio. Also, use of additives like Et_3N or pyridine does not improve the ratio and

slow down the reaction. The use of propargyliodide **2.5c** considerably decreases the yield of the reaction and does not improve the product ratio (Scheme 2.28).

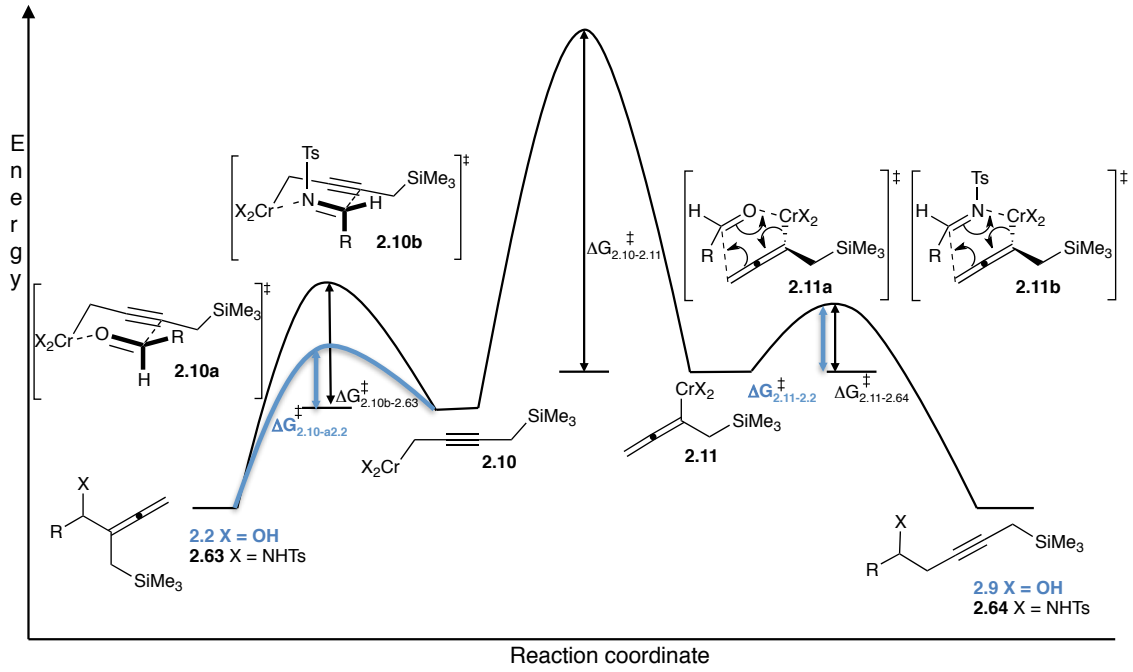
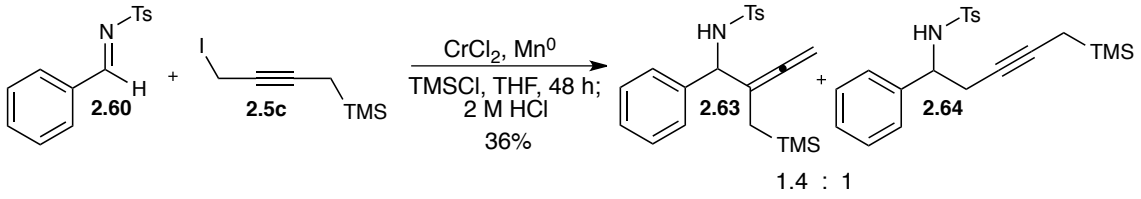


Figure 2.3. Reaction diagram for the chromium-catalyzed allenylation.

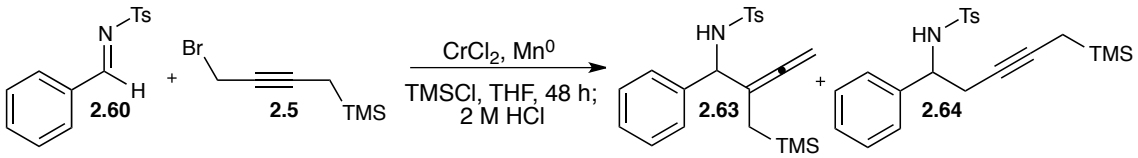
Scheme 2.28. Allenylation of tosyl imine with propargyl iodine **2.5c.**



To discard the possibility of an isomerization process occurring under the reaction conditions, pure allene **2.63** was stirred with propargyl bromide in the presence of the catalytic

Cr^{+1}/Mn^0 system followed by usual workup. After this process, the corresponding alkyne was not observed by ^1H NMR spectroscopy. (Scheme 2.29).

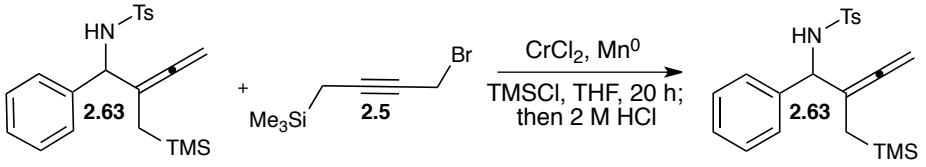
Table 2.18. Optimization of allenylation conditions.[a]



entry	$CrCl_2$ (%)	temperature (°C)	conversion (%)[b]	ratio (**2.63:2.64**)[b]
1	5	r.t.	87	1:1
2	10	r.t.	99	2.5:1
3	15	r.t.	91	2.6:1
4[c]	30	r.t.	99	3.5:1
5	50	r.t.	99	3.5:1
6	10	0	27	0:1
7	10	70	99	2:1
8[d]	30	r.t.	23	2:1
9[e]	30	r.t.	82	2.5:1
10[f]	30	r.t	91	1:1.6

[a] Imine (1 equiv), propargyl bromide **2.5** (1.5 equiv), $CrCl_3$ (30 mol%), Mn (2 equiv), TMSCl (1.1 equiv), 48 h; then 1 M HCl (2 mL) [b] Determined by ^1H NMR Spectroscopy. [c] Propargyl bromide (2 equiv). [d] Solvent: CH_3CN. [e] Mn (5 equiv). [f] Propargyl bromide (3 equiv), reaction time: 16 h.

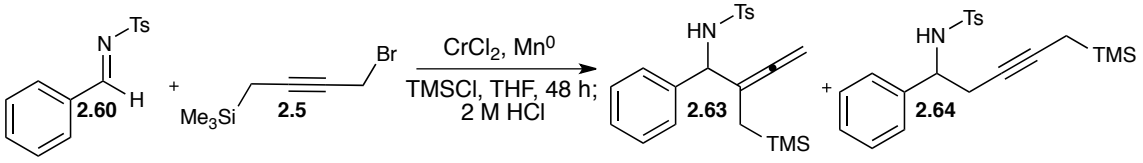
Scheme 2.29. Treatment of allene **2.63** with propargyl bromide **2.5.**



The reaction conditions can be tailored to afford propargylic amine **2.64** as the major product. The formation **2.64** is favored when the amount of catalyst if reduced. Absence of

TMSCl, use of TESCl or large excess of manganese also favor the formation of this regiosomer (Table 2.19). This effect is equally observed when propargyl bromide **2.65,** containing a DMPS group is used. (Table 2.20)

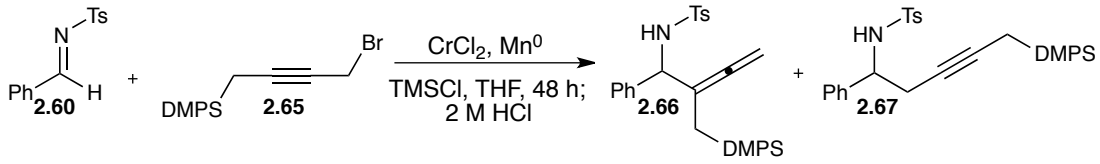
Table 2.19. Optimization towards the synthesis of propargylic amine.[a]



entry	$CrCl_2$ (%)	conversion (%)[b]	ratio (**2.63:2.64**)[b]
1[c]	10	95	1:2.5
2[d]	10	95	1:2.5
3[e]	10	95	1:1.3
4[f]	10	70	1:1.7

[a] Imine (1 equiv), propargyl bromide **2.5** (1.5 equiv), $CrCl_3$ (10 mol%), Mn (2 equiv); then 1 M HCl (2 mL). [b] Determined by ^{1}H NMR Spectroscopy. [c] No TMSCl added. [d] TESCl (1.1 equiv). [e] TESCl (4 equiv). [f] Mn (5 equiv), TMSCl (1.1 equiv).

Table 2.20. Use of (4-bromobut-2-yn-1-yl)dimethyl(phenyl)silane for the synthesis of allenic and propargylic amines.[a]

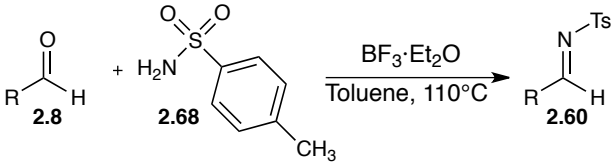


entry	$CrCl_2$ (%)	ratio (**2.66:2.67**)[b]	yield (%)[b]
1	30	3:1	52
2[c]	10	1:3.3	42

[a] Imine (1 equiv), propargyl bromide **2.65** (1.5 equiv), Mn (2 equiv), 16 h; then 2 M HCl (2 mL). [b] Determined by ^{1}H NMR Spectroscopy. [c] No TMSCl added.

After optimizing the reaction conditions, different tosyl imines were prepared to examine the scope of the reaction. As described in Table 2.21, Lewis acid $BF_3{\cdot}Et_2O$ was used for the synthesis of *p*-toluenesulfonamides **2.60**. This is an efficient procedure for the synthesis of variety of aromatic and α,β-unsaturated imines. On the contrary, aliphatic imine **2.60f** was not obtained, presumable due to the formation of the corresponding enol from 3-phenylpropanal. The hindered aldehyde *p*-methylbenzalhyde did not afford the desired product under these conditions, giving only a mixture of the imine and the corresponding starting material after several days.

Table 2.21. Lewis acid mediated synthesis of N-tosyl imines.[a]



entry	R		yield (%)[b]
1[c]	Ph	**2.60a**	90
2	4-Br C_6H_4	**2.60b**	53
3	4-CF_3 C_6H_4	**2.60c**	31
4	4-OMe C_6H_4	**2.60d**	85
5	C_6H_5CHCH	**2.60e**	25
6	$PhCH_2CH_2$	**2.60f**	--
7	2-$CH_3C_6H_4$	**2.60g**	--
6	2-Br C_6H_4	**2.60h**	81

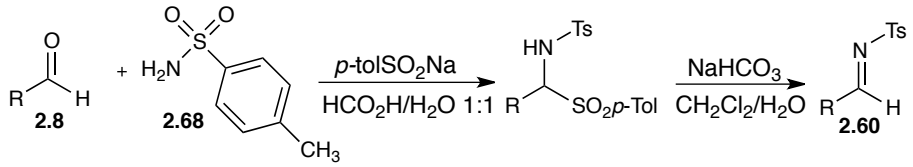
[a]Aldehyde (1 equiv), *p*-toluenesulfonamide (1 equiv), $BF_3{\cdot}OEt_2$ (20% wt). [b] Isolated yield. [c] No $BF_3{\cdot}Et_2O$ added.

Imines **2.60f** and **2.60g** were obtained from the reaction of sodium *p*-toluenesulfinate, *p*-toluenesulfonamide and the corresponding aldehyde to give and intermediate sulfonamide sulfone that upon treatment with base afford the desired aducts. (Table 2.22)[71] While aliphatic

imine 2.60f was obtained after 16 hours, the formation of hindered imine **2.60f** required several days.

In search of a more efficient procedure for the isolation of **2.63**, the mixture of regioisomers was treated with TBAF. After 10 min, **2.64** reacted with TBAF to give the corresponding allene **2.69**, while desilylation of more hindered allene **2.63** requires more than 20 hours. The resulting mixture of allenes is easily separated with column chromatography (Scheme 2.30).

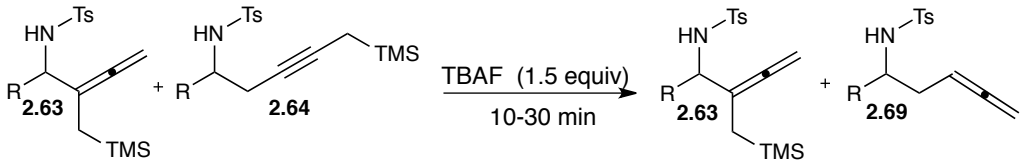
Table 2.22. Preparation of N-tosyl imines.[a]



entry	R		yield (%)[b]
1[c]	$PhCH_2CH_2$	**2.60f**	74
2[d]	2-$CH_3C_6H_4$	**2.60g**	49

[a] Aldehyde (1 equiv), Sodium *p*-toluenesulfinate (1 equiv) *p*-toluenesulfonamide (1 equiv), formic acid (15 mL), H_2O (15 mL) [b] Isolated yield. [c] Reaction time: 16 hours. [d] Reaction time: 5 days.

Scheme 2.30. Desilylation of propargyl amine.



The desired allenic amines were obtained from a variety of tosyl imines. Aromatic imines give the corresponding adducts in good yields (Table 2.23, entries 1 and 2). Imine **2.60c**,

containing an electron-withdrawing group, is consumed after 16 hours under the reaction conditions albeit affording allene **2.63c** in low yield (entry 3). The presence of an electron-donating group in the substrate increases the reaction time, thus allene **2.63d** was obtained in 53% yield after 3 days (entry 4). α,β-unsaturated imine **2.63e** is a poor substrate for the allenylation reaction giving the corresponding allene in only 16% yield (entry 5). On the contrary, aliphatic allene was obtained in excellent yield. The presence of an *o*-bromo substituend dramatically affects the outcome of the reaction. When imine **2.63h** was used, only traces of the desired allene were observed by crude ^{1}H NMR, the possibility of side reaction derived from the catalyst insertion to the arylhalide position is not discarded.

After screening several imines, it was confirmed that the nature of the substituent in the imine has a dramatic effect in the regioselectivity of the reaction (Scheme 2.27). When aliphatic tosyl imine **2.60f** was used, allene **2.60f** was obtained as the major isomer with a 10:1 ratio. On the contrary, sterically hindered imine **2.63g** afforded a 1.3:1 mixture of regioisomers (Scheme 2.31).

Scheme 2.31. Poor regioselectivity in the synthesis of allene **2.63g.**

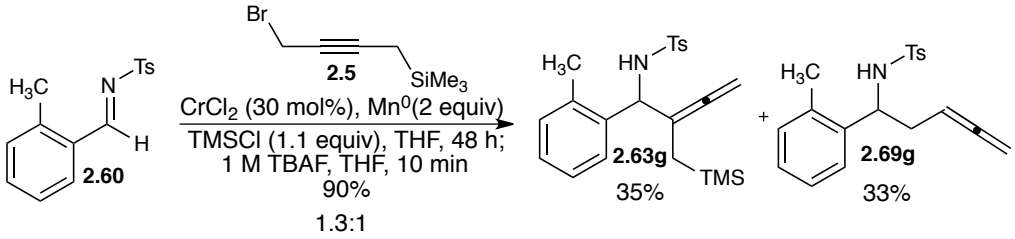
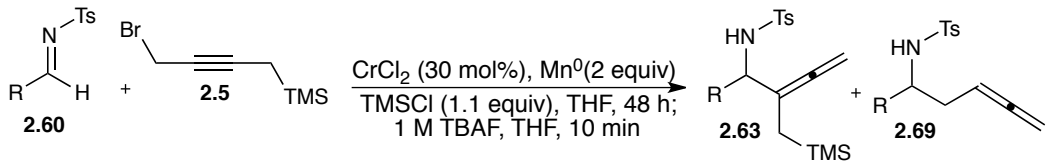
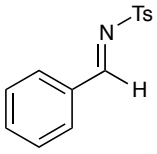
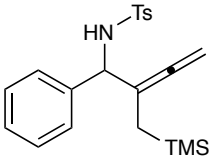
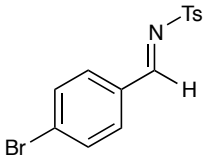
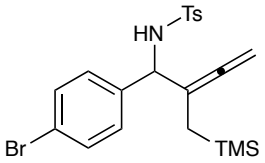
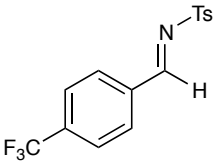
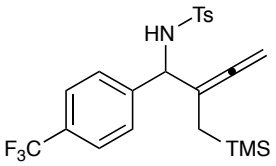
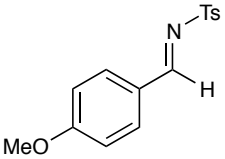
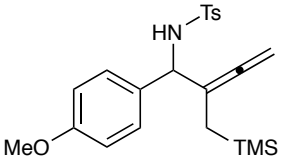
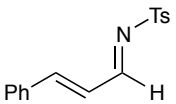
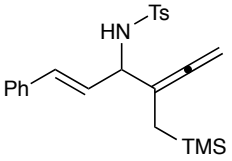
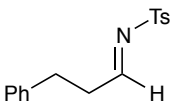
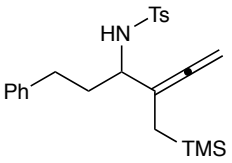
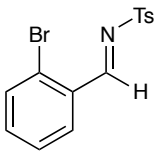
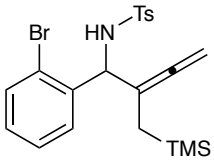


Table 2.23. Synthesis of allenic sulfonamides.[a]

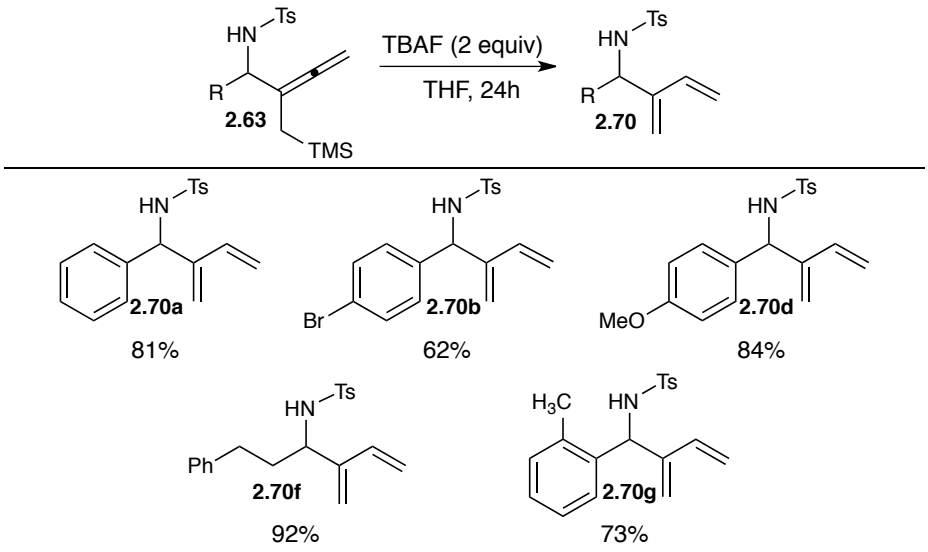


entry	substrate	product		conversion to **2.63**(%)[b]	yield (%)[c]
1			**2.63a**	78	73
2			**2.63b**	73	56
3			**2.63c**	38	25
4[d]			**2.63d**	56	53
5			**2.63e**	-	16
6			**2.63f**	91	84
7			**2.63h**	--	--

[a] Imine (1 equiv), propargyl bromide **2.5** (2 equiv), $CrCl_3$ (30 mol%), Mn (2 equiv), TMSCl (1.1 equiv), 48 h; then TBAF(1 M in THF, 1.5 equiv). [b] Determined by ^{1}H NMR [c] Isolated yield. [d] Reaction time: 3 days, propargyl bromide (3 equiv), 1 equiv added after 48 hours.

Having completed the synthesis of (silylmethyl)allenic amines, 2-aminomethyl-1,3-dienes were successfully prepared using TBAF in good to excellent yields (Table 2.24). This method was equally efficient for desilylation of aromatic an aliphatic allenic amines. 2-aminomethyl-1,3-diene was obtained in 62% yield albeit a 74% conversion. This reaction was not allowed to go to completion to avoid decomposition of the product. Electron rich diene **2.70d** was obtained in 84% yield. Finally, allenic imine **2.63g** afforded the desired diene albeit the presence of an ortho-substituent.

Table 2.24. Synthesis of 2-aminomethyl-1,3-dienes. [a]



[a] Allene (1 equiv) TBAF (1M in THF, 1 equiv and one more equiv after 3 h). Isolated yields

(silylmethyl)allenes are known to react with several electrophiles including acyl iminium ions[44b], halogens[41d, 72], aldehydes and acetals[44d] to afford highly functionalized dienes (Scheme 2.32). To further illustrate the usefulness of (silylmethyl)allenes **2.63** for the synthesis of highly functionalized 1,3-dienes, allenic amine **2.63a** was mixed with different electrophiles in the

presence of a Lewis acid. (Table 2.25) The corresponding dienes were not obtained in the presence of benzaldehyde or 3-phenylpropanal. However, the desired product was formed in 46% conversion using (dimethoxymethyl)benzene and $TiCl_4$ as a Lewis acid. Under these conditions the cyclization product of **2.73a** may be formed thus, a milder Lewis acid was used to promote the dienyllation reaction. To increase the yield of the reaction and avoid the formation of by-products, $BF_3{\cdot}OEt_2$ was used to afford diene **2.73a** in 100% conversion.

Scheme 2.32. Versatility of allenylsilanes.[41d, 44b, 44d, 72]

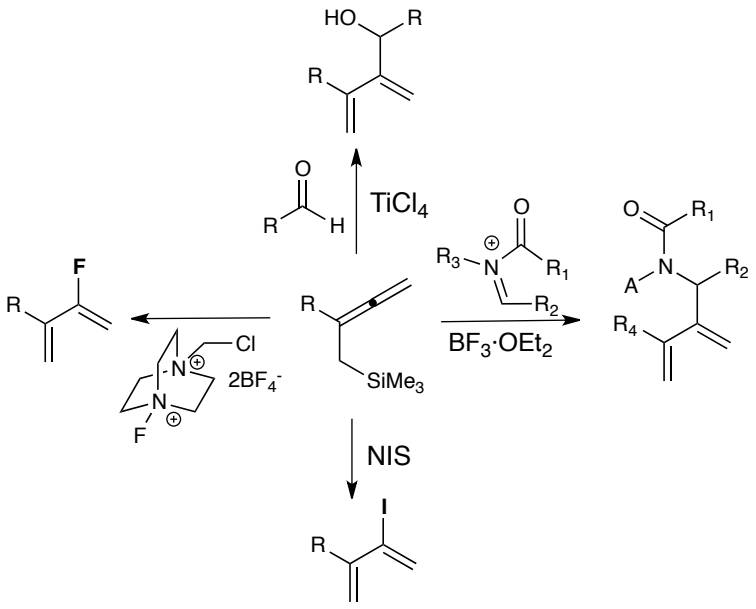
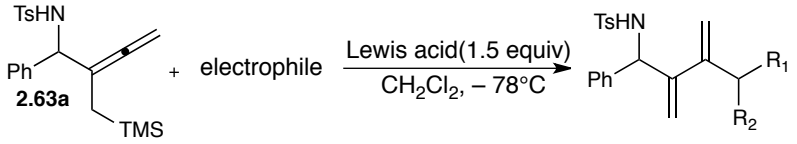
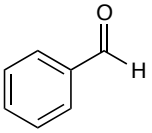
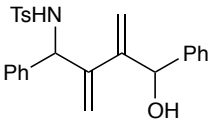
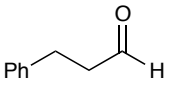
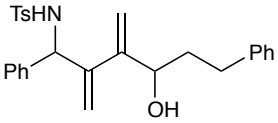
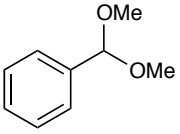
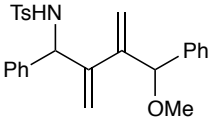
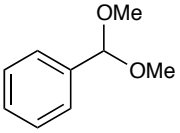
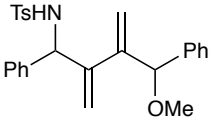


Table 2.25. Synthesis of highly functionalized 1,3-dienes.[a]

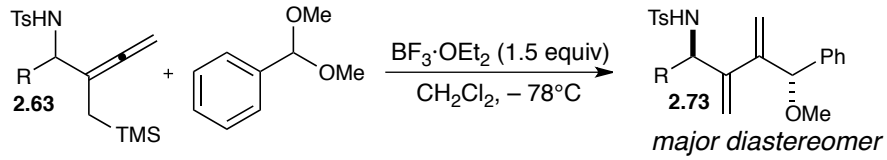


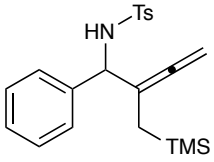
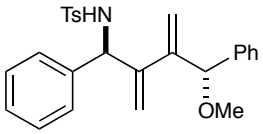
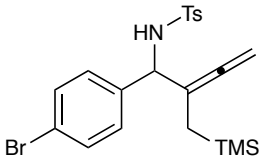
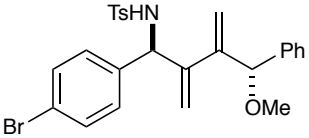
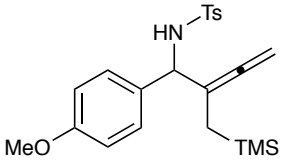
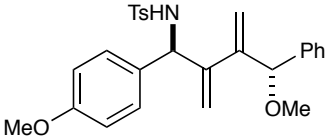
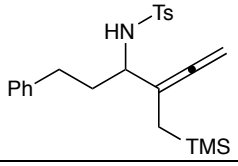
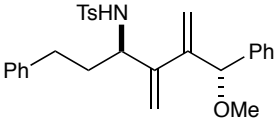
entry	Electrophile	Lewis acid	product		conversion(%)[b]
1		$TiCl_4$		**2.71**	-
2		$TiCl_4$		**2.72**	-
3		$TiCl_4$		**2.73a**	46
4		$BF_3{\cdot}Et_2O$		**2.73a**	100

[a] Imine (1 equiv), aldehyde/acetal (1.6 equiv), Lewis acid (1.5 equiv), – 78°6. [b] Determined by ^{1}H NMR Spectroscopy.

To study the scope of this dienylation reaction, allenic sulfonamides were added to (dimethoxymethyl)benzene in the presence of one equivalent of $BF_3{\cdot}OEt_2$ at – 78 °C. The desired products were obtained after 2-3 hours in excellent yields for aromatic or aliphatic substrates. A 1:3 diasteromeric mixture was obtained for the aromatic substrates (Table 2.26, entries 1-3). While aliphatic substrate **2.63f** afforded the desired diene in a 1:9 d.r. As shown in Scheme 33, addition of allylsilane to aldehydes in the presence of $BF_3{\cdot}OEt_2$ favors the formation of 1,4-*anti* homoallylic alcohols as the major isomer.[73] Thus, the *anti* diastereomer is expected to be the major product for this dienylation reaction.

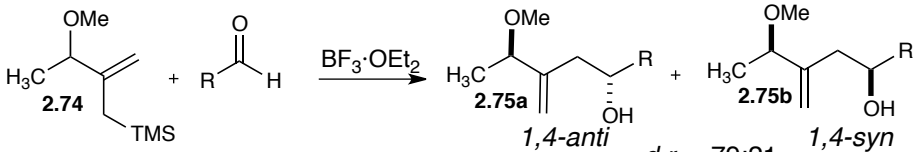
Table 2.26. Synthesis of highly functionalized 1,3-dienes.[a]



entry	substrate	product		yield (%)[b]	*d.r.*[c]
1			**2.73a**	92	1:3
2			**2.73b**	93	1:3
3			**2.73c**	95	1:3
4			**2.73d**	78	1:9

[a] Imine (1 equiv), aldehyde/acetal (1.6 equiv), $BF_3{\cdot}OEt_2$ (1.5 equiv), – 78° C
[b] Isolated yields. [c]Determined by ^1H NMR spectroscopy.

Scheme 2.33. Diastereoselective addition of allylsilane **2.74** to aldehydes.[73a]



R= *p*-$O_2NC_6H_4$
R= C_7H_{15}

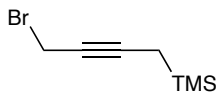
2.5 Experimental procedures and characterization data

2.5.1 General information

All reactions were performed under an argon atmosphere in oven-dried glassware with magnetic stirring. Acetonitrile, propionitrile, DME, TMSCl and DIPEA were distilled from CaH_2 before use. THF, CH_2Cl_2 and Toluene were dried with a solvent purification system. Liquid aldehydes were distilled under reduced pressure and stored refrigerated. Other commercially available reagents were used as received. Reactions were monitored by analytical thin layer chromatography using 0.25 mm glass-backed silica gel plates. Flash column chromatography was performed using silica gel (230-400 mesh). Visualization was accomplished by UV light and potassium permanganate or *p*-anisaldehyde stains.

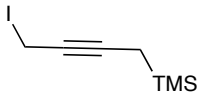
^{1}H NMR spectra were recorded at 300 MHz and referenced to $CDCl_3$ (δ 7.27). ^{1}H NMR coupling constants (*J*) are reported in Hertz (Hz) and multiplicities are indicated by: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), oct (octet) m (multiplet), dt (doublet of triplets), td (triplet of doublets), tt(triplet of triplets), qd (doublet of quadruplets), br (broad), dd (doublet of doublets). Proton-decoupled ^{13}C NMR spectra were recorded at 75 MHz and reported relative to $CDCl_3$ (δ 77). Infrared Spectra were obtained as thin film on NaCl plates. High performance liquid chromatography was performed on a system equipped with a wavelength detector and chiral stationary columns (0.46 cm x 25 cm).

2.5.2 Synthesis of propargyl halides

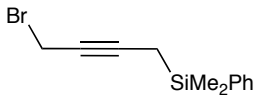


(4-bromobut-2-yn-1-yl)trimethylsilane (2.5): Prepared following the procedure reported by Tong *et al*.[48] Obtained as a clear oil (2.7 g, 13.3

mmol, 76%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.99 (t, *J* = 2.71 Hz, 2H), 1.56 (t, *J* = 2.83 Hz, 2 H), 0.14 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 86.9, 74.2, 16.8, 7.5, -1.9.



(4-iodobut-2-yn-1-yl)trimethylsilane (2.5c)[74]: 4-(trimethylsilyl)but-2-yn-1-ol[48] (460 mg, 3.23 mmol) was added to a solution of PPh_3 (1.1 g, 4.2 mmol) in THF. The mixture was cooled to 0°C and NIS (0.87 g, 3.87 mmol) was added in small portions over 5 min. A yellow precipitate was formed immediately. The mixture was stirred at 0 °C for 2 h. Then, hexanes were added (100 mL) and the yellowish solid formed was removed by filtration. The filtrate was passed though a path of silica to afford a pink solution. The solvent was removed under reduced pressure to give a clear oil (184 mg, 0.73 mmol, 22 %) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.96 (t, *J* = 2.95 Hz, 2H), 1.53 (t, *J* = 2.89 Hz, 2 H), 0.11(s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 85.5, 75.07, 7.7, -1.8, -15.1.

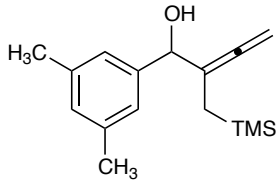


(4-bromobut-2-yn-1-yl)dimethyl(phenyl)silane (2.65): Prepared following the procedure reported by Tong *et al*.[48] Prepared following the procedure reported by Tong *et al*.[48] Obtained as a clear oil (620 mg, 2.3 mmol, 23% over two steps). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.64-7.58 (m, 2H), 7.46-7.37 (m, 2H), 3.96 (t, *J* = 2.91 Hz, 2H), 1.78 (t, *J* = 2.79 Hz, 2 H), 0.41 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.2, 133.6, 129.5, 127.9, 86.4, 74.7, 16.7, 7.1, -3.3; IR (thin film) 3435.7, 3069.7, 2892.9, 222.6 cm^{-1}. MS (ESI) calcd for $C_{12}H_{15}BrSi$ (M - H) 265.0054, found 265.1575.

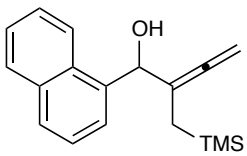
2.5.3 General method for the preparation of allenic alcohols

Inside a nitrogen atmosphere drybox, a mixture of $CrCl_3$ (10 mg, 0.06 mmol) and Mn powder (325-mesh, 22 mg, 0.4 mmol) were added to a 2-dram vial. Then, the vial was capped

with a Teflon lid and it was removed from the drybox. THF (2 mL) was added via syringe and a purple suspension resulted. This was followed by addition of (4-bromo-2-butyn-1-yl)trimethylsilane **2.5** (88 mg, 0.33 mmol), the aldehyde (0.3 mmol) and TMSCl (42 μL, 0.23 mmol). The mixture was stirred at room temperature until the reaction was completed as judged by TLC. HCl (1 M) was added to the gray solution and it was stirred until the alcohol is completely deprotected as judged by TLC. The mixture was then extracted with EtOAc. The mixed organic phases were washed with brine, dried with Mg_2SO_4 and concentrated under reduced pressure to give dark yellow oil. The residue was purified by flash chromatography using ethyl acetate : hexanes (1 : 50 to 1:9) as eluent.

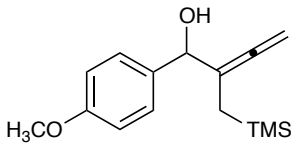


1-(3,5-dimethylphenyl)-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol (2.2i): Obtained as a yellow oil (47 mg, 0.18 mmol, 59%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.98 (s, 2 H), 6.94 (s, 1 H), 5.03 (q, *J* = 3.0 Hz, 2 H), 4.90 (m, 1 H), 2.33 (s, 6 H), 2.21 (d, *J* = 4.8 Hz 1 H), 1.30-1.22 (dt, *J* = 23.0, 15.0 Hz, 1 H), 1.04-0.96 (dt, *J* = 2.8, 14.8 Hz, 1 H), 0.02 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.6, 142.9, 139.0, 130.7, 126.0, 125.9, 106.3, 81.0, 75.9, 22.4, 18.0, -0.0. IR (thin film) 3417.37, 2953.26, 1953.07, 1247.94 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{24}OSi$ (M^+H) 261.1675, found 261.1668.



1-(naphthalen-2-yl)-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol (2.2j): Obtained as a light yellow oil (51 mg, 0.18 mmol, 60%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.24 (d, *J* = 8.3 Hz, 1 H), 7.88 (d, *J* = 8.3 Hz, 1 H), 7.82 (d, *J* = 8.3 Hz, 1 H), 7.64 (d, *J* = 6.2 Hz, 1 H), 7.51 (m, 3 H), 5.78 (m, 1 H), 5.01 (q, *J* = 2.8, 2.8 Hz, 2 H), 2.31 (d, *J* = 4.5 Hz 1 H), 1.43-1.36 (dt, *J* = 2.9, 15.1 Hz, 1 H), 1.13-1.05 (dt, *J* = 2.9, 15.1 Hz, 1 H), 0.0 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.0, 137.1, 134.2, 131.6, 128.9,

128.8, 126.3, 125.8, 125.4, 125.1, 124.2, 104.8, 79.6, 73.0, 17.0, -0.8. IR (thin film) 3385.8, 3060.91, 2953.19, 1952.50, 1247.59, 1056.43 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{22}OSi$ (M+ Li) 289.1600, found 289.1594.

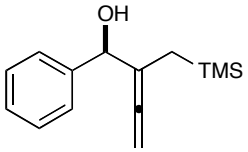


1-(4-methoxyphenyl)-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol (2.2k): $CrCl_2$ (2.5 mg, 0.02 mmol), Mn powder 325-mesh (22 mg, 0.4 mmol), (4-bromo-2-butyn-1-yl)trimethylsilane (45 mg, 0.22 mmol), aldehyde (27 mg, 0.2 mmol), TMSCl (24 mg, 0.22). Title compound was obtained as yellow oil (30 mg, 0.11 mmol, 56%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.32–7.28 (d, *J* = 8.8 Hz, 2 H), 6.91-6.87 (d, *J* = 8.8 Hz, 2 H), 5.01 (q, *J* = 2.8 Hz, 2 H), 4.94 (m, 1 H), 3.82 (s, 3 H), 2.23 (s br, 1 H), 1.31-1.23 (dt, *J* = 2.9, 15.0 Hz, 1 H), 1.06-0.98 (dt, *J* = 2.9, 15.0 Hz, 1 H), 0.02 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 159.5, 134.3, 128.5, 113.9, 105.6, 80.1, 74.6, 55.5, 17.3, -0.8; IR (thin film) 3427.97, 2954.02, 1952.94, 1248.11, 1117.7 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{22}O_2Si$ (M+ Li) 269.1549, found 269.1543.

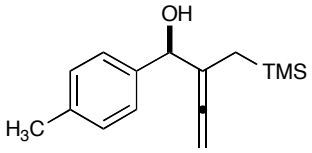
2.5.4 General method for the preparation of enantioenriched allenic alcohols

Inside a nitrogen atmosphere drybox, a mixture of $CrCl_2$ (1.2 mg, 0.01 mmol), Mn powder 325 mesh (22 mg, 0.4 mmol), and carbazole ligand **2.4b** (5.5 mg, 0.01 mmol) were added to a 2-dram vial. Then, the vial was capped with a teflon lid and it was removed from the drybox. Freshly distilled CH_3CN (2 mL) was added via syringe and a yellow suspension resulted. This was followed by addition of *i*-Pr_2NEt (10 μL, 0.06 mmol) and the mixture was stirred for 5 min. After this time, (4-bromo-2-butyn-1-yl)trimethylsilane (61 mg, 0.3 mmol) was added and the solution was allowed to stir for 30 min. Next, the aldehyde (0.2 mmol) and TMSCl (28 μL, 0.22 mmol) were successively added at 0 °C. The mixture was stirred at room

temperature for 48 h or until the reaction was completed as judged by TLC. 1 M HCl was added and the obtained green solution was stirred until the alcohol is completely deprotected as judged by TLC. The mixture was then extracted with EtOAc. The mixed organic phases were washed with brine, dried with Mg_2SO_4 and concentrated under reduced pressure to give a dark orange oil. The residue was purified by flash chromatography using EtOAc:hexanes (1:50 to 1:9) as eluent.

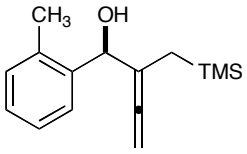


(*R*)-1-phenyl-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol ((–)-2.2a)[41d]**:** Obtained as a clear oil (40 mg, 0.17 mmol, 88%, 78% *ee*) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36-7.27 (m, 5 H), 4.98 (m, 3 H), 2.23 (d, *J* = 4.5 Hz 1 H), 1.30-1.23 (dt, *J* = 2.4, 15.3 Hz, 1 H), 1.07-0.94 (dt, *J* = 2.6, 14.2 Hz, 1 H), 0.0 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.7, 141.9, 128.3, 127.8, 127.0, 105.1, 79.7, 74.9, 16.8, -1.1. IR (thin film) 3387, 3029, 2954, 1952, 1247 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{20}OSi$ (M–OH) 215.1251, found 215.1252; Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes : isopropanol = 98:2, flow rate = 0.6 mL/min) retention time: = 14.3 min (major), 13.0 (minor). $[\alpha]_D^{23}$ –107.2 (*c* 1.0, $CHCl_3$).

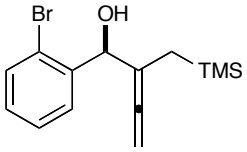


(*R*)-1-*p*-tolyl-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol((–)-2b): Obtained as a clear oil (27 mg, 0.17 mmol, 75%, 70% *ee*) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.29-7.24 (d, *J* = 8.0 Hz, 2 H), 7.19-7.14 (d, *J* = 8.0 Hz, 2 H), 5.01 (q, *J* = 2.8 Hz, 2 H), 4.94 (m, 1 H), 2.36 (s, 3 H), 2.23 (d, *J* = 4.5 Hz 1 H), 1.30-1.23 (dt, *J* = 2.7, 15.0 Hz, 1 H), 1.05-0.97 (dt, *J* = 2.8, 15.0 Hz, 1 H), 0.0 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 139.0, 137.5, 129.0, 126.9, 105.2, 79.7, 74.7, 21.2, 17.0, -1.0. IR (thin film) 3408, 2953, 1953, 1247 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{22}OSi$ (M+Li)

253.1600, found 253.1596; Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes:isopropanol = 98:2, flow rate = 0.6 mL/min) retention time: = 17.8 min (major), 14.0 (minor). $[\alpha]_D^{18}$ –106.7 (*c* 1.0, $CHCl_3$).

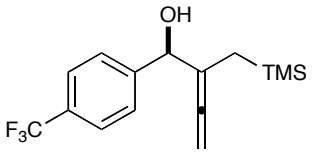


(*R*)-1-*o*-tolyl-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol ((–)-2c): Obtained as a clear oil (38 mg, 0.15 mmol, 77%, 59% *ee*) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.41 (m, 1 H), 7.18 (m, 3 H), 5.24 (m, 1 H), 4.94 (q, *J* = 3.0 Hz, 2 H), 2.37 (s, 3 H), 2.07 (d, *J* = 4.8 Hz 1 H), 1.36-1.28 (dt, *J* = 2.9, 15.1 Hz, 1 H), 1.06-0.99 (dt, *J* = 2.9, 15.1 Hz, 1 H), 0.02 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.4, 139.5, 136.3, 130.5, 127.6, 126.7, 125.9, 104.1, 79.2, 72.1, 19.3, 16.5, -1.1 IR (thin film) 3358, 2953, 1955, 1247 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{22}OSi$ (M+Li) 253.1600, found 253.1597; Enantiomeric excess determined by HPLC (210 nm) using a ChiralPAK AD-H column (hexanes:isopropanol = 98:2, flow rate = 0.6 mL/min) retention time: 12.8 min (major), 11.3 (minor). $[\alpha]_D^{19}$ –49.3 (*c* 1.0, $CHCl_3$).

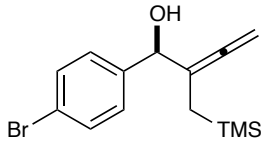


(*S*)-1-(2-bromophenyl)-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol ((–)-2c): Obtained as a yellow oil (44 mg, 0.14 mmol, 82%, 68% *ee*) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.52-7.44 (m, 2 H), 7.33 (td, *J* = 1.57, 7.67 Hz, 1 H), 7.33 (td, *J* = 1.92, 7.67 Hz, 1 H), 5.42 (m, 1 H), 4.94 (q, *J* = 3.09 Hz, 2 H), 2.29 (d, *J* = 6.95 Hz 1 H), 1.39-1.33 (dt, *J* = 2.8, 15.0 Hz, 1 H), 1.16-1.08 (dt, *J* = 2.6, 15.0 Hz, 1 H), 0.0 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.4, 141.0, 132.8, 129.1, 128.8, 127.6, 123.7, 104.16, 79.7, 73.7, 16.8, -1.1 . IR (thin film) 3384, 2953, 1953 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{19}BrOSi$ (M–OH) 293.0356, found 293.0348; Enantiomeric excess determined by HPLC (250 nm) using a

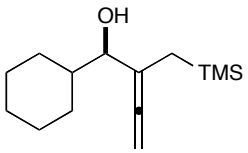
ChiralPAK AD-H column (hexanes:isopropanol = 98:2, flow rate = 0.6 mL/min) retention time: = 15.5 min (major), 13.9 (minor). $[\alpha]_D^{23}$ –74.5 (*c* 1.0, $CHCl_3$).



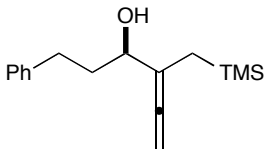
(*R*)-1-(4-(trifluoromethyl)phenyl)-2-((trimethylsilyl)methyl)-buta-2,3-dien-1-ol ((–)-2e): Obtained as a yellow oil (53mg, 0.17 mmol, 88%, 72% *ee*) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.64-7.58 (d, *J* = 8.4 Hz, 2 H), 7.52-7.46 (d, *J* = 8.4 Hz, 2 H), 5.06 (m, 1 H), 5.00 (q, *J* = 2.8, 2.9 Hz, 2 H), 2.31 (d, *J* = 4.75 Hz, 1 H), 1.29-1.21 (dt, *J* = 2.9, 15.1 Hz, 1 H), 1.06-0.98 (dt, *J* = 2.9, 15.1 Hz, 1 H), 0.02 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.9, 146.06, 127.28, 125.22 (q, *J* = 3.72), 104.69, 79.94, 74.63, 16.46, -1.15; IR (thin film) 3307, 2956, 2895, 1951, 1326, 1249 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{19}F_3OSi$ (M+Li) 307.1317, found 307.1320; Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes:isopropanol = 98:2, flow rate = 0.6 mL/min) retention time: = 13.55 min (major), 10.17 (minor). $[\alpha]_D^{23}$ –101.9 (*c* 1.0, $CHCl_3$).



***(R)*-1-(4-bromophenyl)-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol ((–)-2f):** Obtained as a clear oil (37 mg, 0.12 mmol, 60%, 74% *ee*) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.48-7.44 (d, *J*= 8.559 Hz, 2 H), 7.25-7.21 (d, *J* = 8.37 Hz, 2 H), 4.98 (q, *J* = 3.2 Hz, 2 H), 4.94 (m, 1 H), 2.21 (d, *J* = 4.4 Hz 1 H), 1.28-1.20 (dt, *J* = 2.7, 15.1 Hz, 1 H), 1.04-0.96 (dt, *J* = 2.8, 15.0 Hz, 1 H), -0.03 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 141.0, 131.3, 128.8, 121.6, 104.9, 80.1, 74.4, 16.6, -0.9 d. IR (thin film) 3422, 2953, 1952, 1247 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{19}BrOSi$ (M–H) 309.0310, found 309.0314; Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes:isopropanol = 98:2, flow rate = 0.6 mL/min) retention time: = 18.4 min (major), 14.6 (minor). $[\alpha]_D^{20}$ –69.8 (*c* 1.0, $CHCl_3$).



(*R*)-1-cyclohexyl-2-((trimethylsilyl)methyl)buta-2,3-dien-1-ol ((–)-2g): Obtained as a light yellow oil (32 mg, 0.14 mmol, 67%, 68% *ee*) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.80 (q, *J* = 2.8 Hz, 2 H), 3.67 (m, 1 H), 1.79-0.81 (m, 13 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.4, 104.5, 79.4, 77.6, 42.3, 31.1, 28.1, 27.5, 27.4, 27.1, 17.7, 0.05 IR (thin film) 3415, 2925, 2852, 1952, 1247 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{26}OSi$ (M–OH) 221.1720 found 221.1725; Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes:isopropanol = 98:2, flow rate = 0.6 mL/min) retention time: = 8.14 min (major), 8.7 (minor). $[\alpha]_D^{20}$ –15.7 (*c* 1.0, $CHCl_3$).

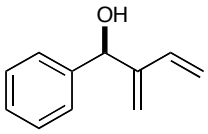


(*R*)-1-phenyl-4-((trimethylsilyl)methyl)hexa-4,5-dien-3-ol ((–)-2h)[41d]: Obtained as a yellow oil (30 mg, 0.11 mmol, 58%, 55% *ee*) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.28-7.13 (m, 5 H), 4.83 (q, *J* = 2.7, 2.6 Hz, 2 H), 3.89 (m, 1 H), 2.8-2.57 (m, 2 H), 2.00-1.87 (m, 1 H), 1.84-1.7 (m, 1 H), 1.57 (s br, 1 H), 1.42-1.34 (dt, *J* = 2.8, 14.9 Hz, 1 H), 1.24-1.15 (dt, *J* = 2.9, 15.9 Hz, 1 H), 0.0 (s, 9 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.8, 142.36, 128.7, 128.62, 216.0, 104.8, 79.0, 72.2, 37.4, 32.1, 17.1, -0.8. IR (thin film) 3362, 2951, 1951, 1247 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{24}OSi$ (M+Li) 267.1756, found 267.1759; Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes:isopropanol = 98:2, flow rate = 0.6 mL/min) retention time: = 15.8 min (major), 14.38 (minor). $[\alpha]_D^{20}$ –5.6 (*c* 1.0, $CHCl_3$).

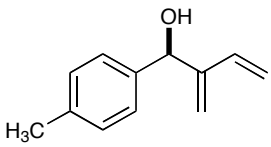
2.5.5 General Method for the preparation of 1,3-butadien-2-ylcarbinols from allenic alcohols

Allene (0.11 mmol) was dissolved in dry THF (1.5 mL). TBAF (1 M wwwin THF, 0.1 mL, 0.1 mmol) was added and the solution was stirred at rt for 36 h. After this time, a saturated

solution of NH_4Cl (3 mL) was added and the mixture was extracted with three portions of ethyl acetate The combined organic fractions were washed with brine, dried over Mg_2SO_4 and concentrated under reduced pressure. The residue was purified by preparative TLC using (1:6) EtOAc:hexanes.

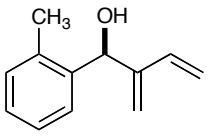


(*S*)-2-methylene-1-phenylbut-3-en-1-ol (2.3a)[75]: Allene **(–)-2.2a** (18 mg, 0.11 mmol), 1 M TBAF in THF (0.1 mL, 0.1 mmol). Title compound was obtained as yellow oil (9 mg, 0.06 mmol, 54%, 70% *ee*). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.35-7.21 (m, 5 H), 6.25 (dd, *J* = 11.5, 17.7 Hz, 1 H), 5.41 (s, 1 H), 5.35 (s, 1 H), 5.27 (s, 1 H), 5.15 (d, *J* = 17.86 Hz, 1 H), 4.98 (d, *J* = 11.23 Hz, 1 H), 2.0 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.4, 141.8, 135.7, 128.4, 127.8, 126.8, 115.7, 115.4, 73.9; IR (thin film) 3362, 3084, 1954, 1817, 1593; HRMS (ESI) calcd for $C_{11}H_{12}O$ (M–OH) 143.0855, found 143.0802; Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AS-H column (hexanes:isopropanol = 98:2, flow rate = 0.6 mL/min) retention time: = 19.55 min (major), 17.87 (minor). $[\alpha]_D^{17}$ –33.5 (*c* 1.0, $CHCl_3$). Reported value (98% *ee*) $[\alpha]_D^{20}$ –93.2 (*c* 1.34, $CHCl_3$)[41c].

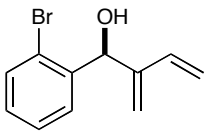


(*S*)-2-methylene-1-p-tolylbut-3-en-1-ol (2.3b)[43d]: Allene **(–)-2.2b** (14 mg, 0.06 mmol), 1 M TBAF in THF (0.6 mL, 0.6 mmol). Title compound was obtained as yellow oil (9 mg, 0.051 mmol, 86%, 65% *ee*) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.30 (d, *J* = 7.90 Hz, 2 H), 7.17 (d, *J* = 7.90 Hz, 2 H), 6.33 (dd, *J* = 10.91, 17.53 Hz, 1 H), 5.45 (s, 2 H), 5.34 (s, 1 H), 5.22 (d, *J* = 18.19 Hz, 1 H), 5.05 (d, *J* = 11.33 Hz, 1 H), 2.36 (s, 3 H), 1.97 (d *J* = 4.83, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.6, 139.0, 137.6, 135.9, 129.2, 126.8, 115.5, 115.3, 73.7, 21.1; IR (thin film) 3363, 2922, 1956, 1905, 1819, 1595 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{14}O$ (M+Li) 181.1205, found 181.1197;

Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AS-H column (hexanes:isopropanol = 98:2, flow rate = 0.6 mL/min) retention time: = 21.17 min (major), 16.7(minor). $[\alpha]_D^{19}$ –51.1 (*c* 1.0, $CHCl_3$). Reported value (89% *ee*) $[\alpha]_D^{24}$ –69.2 (*c* 1.0, $CHCl_3$).[43d]

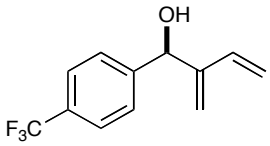


(*S*)-2-methylene-1-*o*-tolylbut-3-en-1-ol (2.3c): Allene **(–)-2.2d** (40 mg, 0.16 mmol), 1 M TBAF in THF (0.16 mL, 0.16 mmol). Title compound was obtained as yellow oil (22 mg, 0.12 mmol, 79%, 68% *ee*.). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.41 (m, 1 H), 7.21 (m, 3 H), 6.40 (dd, *J* = 11.33, 17.80 Hz, 1 H), 5.68 (d, *J* = 4.88 Hz, 1 H), 5.36 (s, 1 H), 5.26 (s, 1 H), 5.21 (d, *J* = 17.55 Hz, 1 H), 5.09 (d, *J* = 11.22 Hz, 1 H), 2.88 (s, 3 H), 1.86 (d, *J* = 4.86, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.1, 139.6, 136.3, 135.8, 130.4, 127.7, 126.2, 126.1, 116.5, 114.9, 70.0, 18.9; IR (thin film) 3407, 2924, 1721, 1461 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{14}O$ (M+Li) 181.1205: found 181.1200. Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes:isopropanol = 98:2, flow rate = 0.6 mL/min) retention time: = 23.5 min (major), 21.6 (minor). $[\alpha]_D^{19}$ – 16.5 (*c* 1.0, $CHCl_3$).

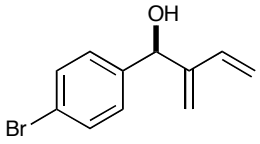


(*S*)-1-(2-bromophenyl)-2-methylenebut-3-en-1-ol (2.3d)[76]: Allene **(–)-2.2d** (43 mg, 0.13 mmol), 1 M TBAF in THF (0.14 mL, 0.14 mmol). Title compound was obtained as yellow oil (27 mg, 0.11 mmol, 82%, 77% *ee*.). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.61 (dd, *J* = 1.22, 7.98 Hz, 1 H), 7.51 (dd, *J* = 1.79, 7.77 Hz, 1 H), 7.35 (dt, *J* = 1.33, 7.42 Hz, 1H), 7.20 (dt, *J* = 1.79, 7.62 Hz, 1H), 6.42 (dd, *J* = 11.33, 18.21 Hz, 1 H), 5.41 (m, 1 H), 5.36 (m, 1 H), 5.25 (dd, *J* = 0.78, 17.90 Hz 1 H), 5.12 (d, *J* = 11.18 Hz, 1 H), 2.17 (d, *J* = 4.27, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.4, 140.7, 136.1, 132.8, 129.4, 128.57, 127.7, 123.8, 116.8, 115.2, 71.9; IR (thin film) 3334, 3088, 2918, 1594 cm^{-1}; MS (APCI)

calcd for $C_{12}H_{14}O$ (M–OH) 221.00, found 221.40. Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes:isopropanol = 98:2, flow rate = 0.6 mL/min) retention time: = 23.5 min (major), 21.6 (minor). $[\alpha]_D^{17}$ –77.4 (*c* 1.0, $CHCl_3$).

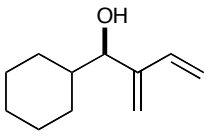


(*S*)-2-methylene-1-(4-(trifluoromethyl)phenyl)but-3-en-1-ol (2.3e): Allene **(–)-2.2e** (26 mg, 0.08 mmol), 1 M TBAF in THF (0.8 mL, 0.08 mmol). Title compound was obtained as yellow oil (11 mg, 0.05 mmol, 59%, 69% *ee*). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.26 (d, *J* = 8.39 Hz, 2 H), 7.53 (d, *J* = 8.39 Hz, 2 H), 6.31 (dd, *J* = 11.56, 17.81 Hz, 1 H), 5.55 (d, *J* = 4.33 Hz, 1 H), 5.38 (s, 1 H), 5.27 (d, *J* = 18.31 Hz, 1 H), 5.10 (dd, *J* = 11.50 Hz, 1 H), 2.08 (d, *J* = 4.066 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.2, 145.7, 135.3, 127.0, 125.4 (q, *J* = 3.94), 116.7, 166.0, 73.6; IR (thin film) 3418, 2923, 2951, 1619, 1325 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{11}F_3O$ (M–H) 227.0654 found 227.0690; Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes:isopropanol = 98:2, flow rate = 0.5 mL/min) retention time: = min 23.45 (major), 19.18 (minor). $[\alpha]_D^{19}$ –10.5 (*c* 1.0, $CHCl_3$).

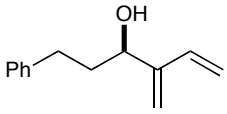


(*S*)-1-(4-bromophenyl)-2-methylenebut-3-en-1-ol (2.3f)[43d]: Allene **(–)-2.2f** (36 mg, 0.11 mmol), 1 M TBAF in THF (0.1 mL, 0.11 mmol). Title compound was obtained as yellow oil (19 mg, 0.08 mmol, 72%, 73% *ee*.). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.48 (d, *J* = 8.55 Hz, 2 H), 7.29 (d, *J* = 9.36 Hz, 2 H), 6.30 (dd, *J* = 11.55, 17.80 Hz, 1 H), 5.45 (s, 1 H), 5.38 (s, 1 H), 5.35 (s, 1 H), 5.23 (d, *J* = 18.13 Hz, 1 H), 5.08 (dd, *J* = 11.29 Hz, 1 H), 1.98 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.3, 140.8, 135.5, 131.6, 128.6, 121.7, 116.2, 115.8, 73.4; IR (thin film) 3356, 2922, 1634, 1486, 1403, 1071 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{11}BrO$ (M–H) 236.9915, found 236.9916;

Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AS-H column (hexanes:isopropanol = 98:2, flow rate = 0.6 mL/min) retention time: = 22.4 min (major), 19.34 (minor). $[\alpha]_D^{19}$ –24.3 (*c* 1.0, $CHCl_3$). Reported value (86% *ee*) $[\alpha]_D^{24}$ – 15.4 (*c* 1.0, $CHCl_3$).[43d]

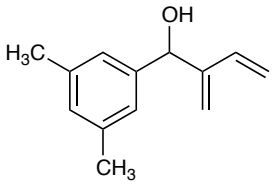


(*R*)-1-cyclohexyl-2-methylenebut-3-en-1-ol (2.3g)[75]: Allene **(–)-2.2g** (25 mg, 0.1 mmol), 1 M TBAF in THF (0.1 mL, 0.1 mmol). Title compound was obtained as yellow oil (14 mg, 0.08 mmol, 84%, 64% *ee*.). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.26 (dd, *J* = 11.06, 17.39 Hz, 1 H), 5.30 (d, *J* = 17.63 Hz 1 H), 5.13 (s, 1 H), 5.07 (s, 1 H), 5.03 (d, *J* = 11.22 Hz, 1 H), 4.06 (d, *J* = 5.99 Hz, 1 H), 1.86-0.87 (m, 12 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.1, 136.2, 114.7, 114.6, 76.9, 41.8, 30.0, 27.7, 26.4, 26.3, 26.1 IR (thin film) 3418, 2924, 2852, 1731 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{18}O$ (M–H) 165.1285, found 165.1093; Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AD-H column (hexanes:isopropanol = 99:1, flow rate = 0.5 mL/min) retention time: = 17.28 min (major), 18.3 (minor). $[\alpha]_D^{19}$ – 2.8 (*c* 1.0, $CHCl_3$). Reported value (89% *ee*) $[\alpha]_D^{20}$ – 6.0 (*c* 3.25, $CHCl_3$).[42a]

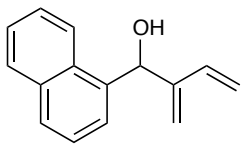


(*R*)-2-methylene-1-*o*-tolylbut-3-en-1-ol (2.3h)[37d]: Allene **(–)-2.2h** (26 mg, 0.09 mmol), 1 M TBAF in THF (0.1 mL, 0.1 mmol). Title compound was obtained as yellow oil (8 mg, 0.04 mmol, 43%, 48% *ee*.). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.44-7.28 (m, 5 H), 6.45 (dd, *J* = 11.6, 18.1 Hz, 1 H), 5.39 (s, 1 H), 5.33 (d, *J* = 18.24 Hz, 1 H), 5.29 (s, 1 H), 5.19 (d, *J* = 11.52 Hz, 1 H), 4.17 (dd, *J* = 4.17, 8.33 Hz, 1 H), 2.48-2.77 (m, 2 H), 2.19-2.07 (m, 1 H), 2.06-1.96 (m, 1 H), 1.76 (s br, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.0, 141.8, 136.0, 128.5, 128.3, 125.8, 114.3, 114.2, 70.6, 37.9, 31.9; IR (thin film) 3396.4, 3026.3, 2924.6, 1713.8 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{14}O$ (M+Li) 195.1361, found 195.1245; Enantiomeric

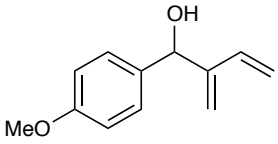
excess determined by HPLC (250 nm) using a Chiralcel OB-H column (hexanes:isopropanol = 99:1, flow rate = 0.5 mL/min) retention time: = 30.21 min (major), 27.46 (minor). $[\alpha]_D^{19}$ + 14.3 (*c* 1.0, $CHCl_3$). Reported value (77% *ee*) $[\alpha]_D^{29}$ + 36.4 (*c* 1, $CHCl_3$).[37d]



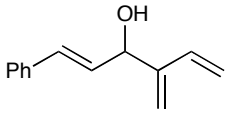
1-(3,5-dimethylphenyl)-2-methylenebut-3-en-1-ol (2.3i): Allene **2.2i** (25 mg, 0.09 mmol), 1 M TBAF in THF (0.09 mL, 0.09 mmol). Compound was obtained as yellow oil (19 mg, 0.07 mmol, 81%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.01 (s, 2 H), 6.94 (s, 1 H) 6.32 (dd, *J* = 11.38, 17.66 Hz, 1 H), 5.45 (s, 1 H), 5.41 (s, 1 H), 5.35 (s, 1 H), 5.24 (d, *J* = 18.09 Hz, 1 H), 5.05 (dd, *J* = 11.30 Hz, 1 H), 2.32 (s, 1 H), 1.94 (s br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 128.3, 141.8, 138.0, 135.9, 129.5, 124.6, 115.3, 73.9, 21.3; IR (thin film) 3356.27, 3008.74, 2918.32, 1608.09 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{16}O$ (M+ Li) 195.1361, found 195.1448.



2-methylene-1-(naphthalen-1-yl)but-3-en-1-ol (2.3j)[6f]: Allene **2.3j** (25 mg, 0.09 mmol), 1 M TBAF in THF (0.16 mL, 0.16 mmol). The title compound was obtained as yellow oil (28 mg, 0.13 mmol, 74%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.13 (d, *J* = 8.97, 1 H), 7.89 (d, *J* = 7.29, 1 H), 7.83 (d, *J* = 8.41, 1 H), 7.63 (d, *J* = 8.41, 1 H), 7.58-7.44 (m, 3 H), 6.47 (dd, *J* = 11.08, 18.20 Hz, 1 H), 6.27 (s, 1 H), 5.43 (s, 1 H), 5.35 (s, 1 H), 5.24 (d, *J* = 19.05 Hz, 1 H), 5.10 (d, *J* = 11.72 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.3, 137.1, 136.4, 133.8, 131.0, 128.8, 128.6, 126.3, 125.6, 125.5, 125.3, 124.4, 123.4, 117.3, 115.1. 69.6; MS (ESI) calcd for $C_{15}H_{14}O$ (M+ Li) 217.1205, found 217.1244.

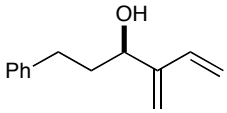


1-(4-methoxyphenyl)-2-methylenebut-3-en-1-ol (2.3k)[6f]**:** Allene **2.2k** (30 mg, 0.11 mmol), 1 M TBAF in THF (0.11 mL, 0.11 mmol). Title compound was obtained as yellow oil (16 mg, 0.082 mmol, 75%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.32 (d, *J* = 8.86 Hz, 2 H), 6.89 (d, *J* = 8.86 Hz, 2 H), 6.32 (dd, *J* = 11.89, 18.42 Hz, 1 H), 5.46 (s, 1 H), 5.44 (s, 1 H), 5.34 (s, 1 H), 5.19 (d, *J* = 18.12 Hz, 1 H), 5.04 (d, *J* = 11.488 Hz, 1 H), 3.809 (s, 3 H), 1.93 (d *J* = 4.0, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.2, 147.6, 135.9, 134.2, 123.2, 115.4, 115.3, 113.9, 73.4, 55.3; IR (thin film) 3416.87, 3004.51, 2959.47, 1824.23, 1610.72, 1510.6, 1249.0, cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{14}O_2$ (M+ Li) 197.1154, found 197.1154.

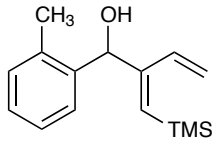


4-methylene-1-phenylhexa-1,5-dien-3-ol (2.3i)[43c]: Inside a Nitrogen atmosphere drybox, $CrCl_2$ (2.5 mg, 0.02 mmol) and Mn^0 powder 325-mesh (22 mg, 0.4 mmol) were added to a 2-dram vial. Then, the vial was capped with a Teflon lid and it was removed from the drybox. Dry THF (2 mL) was added via syringe and a gray suspension was formed. This was followed by addition of 4-bromo-2-butyn-1-yl)trimethylsilane (45 mg, 0.22 mmol), cinnamaldehyde (27 mg, 0.2 mmol) and TMSCl (24 mg, 0.22 mmol). The mixture was stirred at room temperature for 16 h. The mixture is then extracted with three portions of ethyl acetate. The mixed organic phases were washed with brine, dried with Mg_2SO_4 and concentrated under reduced pressure. The residue was redissolved in THF (1.5 mL) and, TBAF (1 M in THF, 0.4 mmol, 0.4 mL) is added. After 36h, a saturated solution of NH_4Cl (3 mL) was added and the mixture was extracted with three portions of ethyl acetate. The combined organic fractions were washed with brine, dried over Mg_2SO_4 and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography using 1:6 ethylacetate:hexanes and it was obtained as a clear oil (13 mg, 0.07 mmol, 35%). ^{1}H NMR

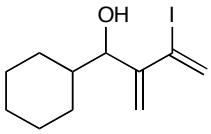
($CDCl_3$, 300 MHz) δ 7.43-7.25 (m, 5 H), 6.70 (d, *J* = 15.93 Hz, 1 H), 6.39 (dd, *J* = 11.36, 17.79 Hz, 1 H), 6.32 (dd, *J* = 6.22, 15.86 Hz, 1 H), 5.46 (d, *J* = 18.33 Hz, 1 H), 5.39 (s, 1 H), 5.27 (s, 1H), 5.17 (d, *J* = 11.25 Hz, 1 H), 5.10 (d, *J* = 6.11 Hz, 1 H), 1.81 (d *J* = 3.29, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.3, 136.5, 135.8, 131.2, 130.2, 128.5, 127.8, 126.5, 115.3, 115.2, 72.2; IR (thin film) 3390, 3027, 2921, 2851, 1494 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{14}O_2$ (M+Li) 193.1205, found 193.1202.



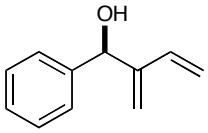
Preparation of (*R*)-2-methylene-1-*o*-tolylbut-3-en-1-ol from 3-phenylpropionaldehyde: Inside a Nitrogen atmosphere drybox, $CrCl_2$ (1.2 mg, 0.01 mmol), Mn^0 powder 325-mesh (22mg, 0.4 mmol), and **2.4b** (5.5mg, 0.01 mmol) were added to a 2-dram vial. Then, the vial was capped with a Teflon lid and it was removed from the drybox. Freshly distilled CH_3CN (2 mL) was added via syringe and a yellow suspension was formed. This was followed by addition of *N*,*N*-diisopropylethylamine (7.5mg, 0.3 mmol) and the mixture was stirred for 5 min. After this time, (4-bromo-2-butyn-1-yl)trimethylsilane **2.5** (50mg, 0.3 mmol) was added and the solution was allowed to stir for 30 min. Next, the aldehyde (0.2 mmol) and TMSCl (24 mg, 0.22 mmol) were successively added at 0 °C. The mixture was stirred at room temperature for 36 h. 2 M HCl (2 mL) was added dropwise to the solution and the mixture was stirred for 5 h. The mixture is then extracted with three portions of EtOAc. The mixed organic phases were washed with brine, dried with Mg_2SO_4 and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography using 1:6 EtOAc:hexanes and it was obtained as a yellow oil (22 mg, 0.11 mmol, 56%, 44% *ee*). Enantiomeric excess determined by HPLC (250 nm) using a Chiralcel OB-H column (hexanes:isopropanol = 99:1, flow rate = 0.5 mL/min) retention time: = 30.21 min (major), 27.46 (minor).



1-o-tolyl-2-((trimethylsilyl)methylene)but-3-en-1-ol (2.24): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.31-7.27 (m, 1 H), 7.09-7.00 (m, 3 H), 5.56 (d, *J* = 2.87 Hz, 1 H), (s, 1 H), 5.37 (d, *J* = 2.87 Hz, 1 H), 4.93 (m, 2H), 2.37 (s, 3 H), 1.76 (d, *J* = 3.76, 1 H), -0.13 (2, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7, 140.6, 136.6, 131.1, 128.4, 128.1, 128.0, 127.5, 126.8, 13.4, 72.2, 20.1, 0.0 IR (thin film) 3374.3, 2955.9, 1619.9, 1486.3, 1248.3 cm^{-1} HRMS (ESI) calcd for $C_{15}H_{22}OSi$ (M + Na) 269.1338, found 269.1334.

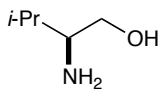


1-cyclohexyl-3-iodo-2-methylenebut-3-en-1-ol (2.25): Allenic alcohol **(–)-2.2g** (20 mg, 0.08 mmol) was dissolved in dry CH_2Cl_2 (1 mL). Then, at 0 °C, a solution of NIS (40 mg, 0.17 mmol) in CH_2Cl_2 (0.5 mL) was added via cannula. The pink solution was stirred at r.t. for 1 h. After this time, 0.16 mL of a TBAF (1 M in THF, 0.16 mmol) was added via syringe and the mixture was stirred for 2 h. After this time, a saturated solution of NH_4Cl was added and the mixture was extracted with three portions of EtOAc. The combined organic phases were washed with brine, dried over Mg_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography using EtOAc:hexanes 1:6 as eluent. The title compound was obtained as a yellow oil (35 mg, 0.12 mmol, 60% yield). ^{1}H NMR δ 6.3 (d, *J* = 1.67 H), 5.91 (d, *J* = 1.46 H), 5.42 (s, 1 H), 5.30 (s, 1 H), 4.28 (t, *J* = 4.75, 1H) 1.73-1.63 (m, 3 H), 1.56 (d, *J* = 5.2, 2H), 1.23-0.89 (m, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.8, 127.8, 118.9, 107.3, 76.3, 41.5, 30.1, 27.7, 26.36, 26.33, 26.0; IR (thin film) 3437, 1926, 2852, 1723, 1260 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_{17I}O$ (M–I) 265.1274, found 265.1274.

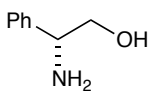


Preparation of (*S*)-2-methylene-1-phenylbut-3-en-1-ol (2.3a) from (S)-1-(4-bromophenyl)-2-methylenebut-3-en-1-ol (2.3f): Compound **2.3f** (16 mg, 0.067 mmol) was dissolved in THF (2 mL) and cooled to –78 °C. Then *n*-BuLi (0.53 mL of 2.5 M solution, 0.13 mmol) was added dropwise and the mixture was stirred for 15 minutes. Water (0.5 mL) was added dropwise and stirred for 5 minutes. The mixture was diluted with ethyl acetate, washed with brine, dried over Mg_2SO_4 and concentrated under reduced pressure. The residue was filtered through a short plug of silica. Compound **2.3a** was obtained as a yellow oil (11 mg, 0.06 mmol, 93% yield, 69% *ee*). $[\alpha]_D^{19}$ – 32.4 (*c* 1.0, $CHCl_3$).

2.5.6 Synthesis of aminoalcohols 2.18



L-valinol (2.18b)[77]: Under argon atmosphere, THF (500 mL) was added to a round bottom flask containing lithium aluminum hydride (15 g, 395 mmol) at 0 °C. Then L-valine (30 g, 356 mmol) was added in small portions over 30 min. The mixture was then allowed to warm to r. t. follow by reflux for 16 h. After this time, the reaction mixture was cooled to 0 °C and diluted with diethyl ether (300 mL). Then 15 % NaOH (20 mL) and water where added slowly. The solution was stirred for 30 min and a white precipitate was formed, which was removed by filtration. The filter cake was washed with diethyl ether. Combined organic filtrates were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by distillation (80-90 °C at 10 Torr). Pure L-valinol was obtained as a clear oil (17.8 g, 172.6 mmol, 67%). $[\alpha]_D^{20}$ + 12.7 (neat).Literature value: $[\alpha]_D^{20}$ + 14.6 (neat).

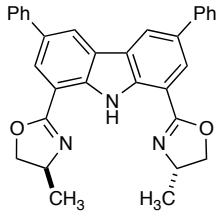


D-phenylglycinol (2.18d)[77]: Prepared following the procedure reported for L-valinol. D-phenylglucine methyl ester (20g, 99 mmol), lithium aluminum hydride

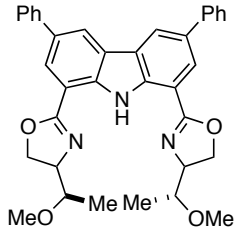
(7.53g, 198 mmol). Compound obtained as white crystals (11.55 g, 84 mmol, 85%). $[\alpha]_D^{19}$ – 36.15 (*c* 0.76, 1 M HCl). Literature value: $[\alpha]_D^{25}$ – 32 (*c* 0.75, 1 M HCl). [78]

2.5.7 General procedure for synthesis of bis(oxazoline) carbazole ligand 2.4 from 1,8-dihalocarbazole 2.17 via Pd–catalyzed carbonylative amidation followed by CH_3SO_2Cl induced cyclization

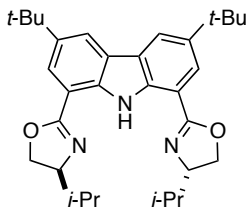
Modified procedures from the literature were used.[50, 79] To a solution of 0.5 mmol of the 1,8-diiodocarbazole and $Pd(PPh_3)_4$ (20 mol%) in 5 mL of dry, degassed DMF was added the corresponding amino alcohol (2.6 equiv) and Et_3N (4 equiv) via a syringe. CO gas was then bubbled through the reaction mixture and a balloon of CO placed over the reaction flask. The reaction mixture was stirred at 60 °C for 8 h. After the mixture was cooled down it was diluted with CH_2Cl_2, washed with brine and 1 M $CuSO_4$ several times. The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure to give the desired bisamide. The bisamide was partially purified by passing through a short silica bed and eluting with CH_2Cl_2 and methanol. The eluent was concentrated under reduced presusre, dried under vacuum and the bisamide thus obtained was dissolved in 3 mL CH_2Cl_2. NEt_3 (2 equiv) was added and the solution was cooled to 0 °C. Methanesulfonyl chloride (2.5 equiv) was added and the reaction mixture was allowed to warm to room temperature and stirred overnight. It was then poured into saturated aq. NH_4Cl, the organic layer was separated and the aqueous layer extracted with CH_2Cl_2. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was treated with 5% methanolic KOH soln. (3 mL) and heated under reflux for 3 h. The solvent was evaporated, residue poured into H_2O and extracted with CH_2Cl_2. The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure to obtain desired product, which was purified by column chromatography.



(4S,4'S)-2,2'-(3,6-diphenyl-9H-carbazole-1,8-diyl)bis(4-methyl-4,5-dihydrooxazole) (2.4a)[47b]: Purification by column chromatography (1:1 CH_2Cl_2 in hexanes) and recrystallization (from hexanes/EtOAc) afforded the product as a yellow solid (121 mg, 0.25 mmol, 48%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.00 (s, 1H) 8.48 (d, J = 1.8 Hz, 2H), 8.22 (d, J = 1.8 Hz, 2H), 7.77-7.80 (m, 4H), 7.49-7.54 (m, 4H), 7.36-7.41 (m, 2H), 4.61-4.70 (m, 4H), 4.05-4.09 (m, 2H), 1.55 (d, J = 6.3 Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 162.6, 141.4, 138.8, 132.5, 128.8, 127.3, 126.7, 125.2, 124.2, 121.9, 110.7, 73.6, 62.3, 21.7.



(4R,4'R)-2,2'-(3,6-diphenyl-9H-carbazole-1,8-diyl)bis(4-((R)-1-methoxyethyl)-4,5-dihydrooxazole) (2.4f): Purification by column chromatography (1 to 3% MeOH in CH_2Cl_2) afforded 61% of the product as a yellow solid. Mp 147-148 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (d, J = 1.5 Hz, 2H), 8.18 (d, J = 1.8 Hz, 2H), 7.71-7.74 (m, 4H), 7.42-7.47 (m, 4H), 7.29-7.35 (m, 2H), 4.64-4.66 (m, 2H), 4.43-4.46 (m, 4H), 3.68-3.71 (m, 2H), 3.44 (s, 6H), 1.31 (d, J = 6.3 Hz, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 163.8, 141.5, 139.1, 132.7, 129.0, 127.5, 126.9, 125.6, 124.4, 122.2, 110.8, 77.8, 70.4, 68.1, 57.3, 14.7; HRMS Calcd for $C_{36}H_{36}N_3O_4$: 574.2706 [M + H]$^+$. Found: 574.2704; $[\alpha]_D^{23}$ + 35.313; (*c* 1.0, $CHCl_3$).

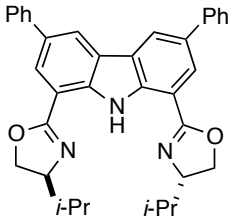


(4S,4'S)-2,2'-(3,6-di-tert-butyl-9H-carbazole-1,8-diyl)bis(4-isopropyl-4,5-dihydrooxazole) (2.4i): Purification by flash chromatography (3:1 CH_2Cl_2 in hexanes) afforded 51% of the product as a yellow solid. mp 178-180 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.80 (s, 1H), 8.30 (d, J =

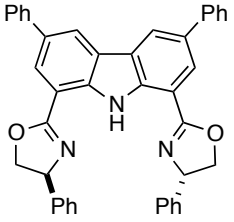
1.5 Hz, 2H), 8.03 (d, *J* = 1.8 Hz, 2H), 4.47-4.56 (m, 2H), 4.19-4.30 (m, 4H), 1.90-1.97 (m, 2H), 1.54 (s, 18H), 1.20 (d, *J* = 6.6 Hz, 6H), 1.07 (d, *J* = 6.6 Hz, 6H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 162.7, 141.5, 137.6, 123.4, 123.2, 119.7, 109.7, 72.9, 69.8, 34.8, 33.4, 32.1, 19.2, 18.7; IR 3354.9, 2959.0, 1649.3, 1487.8, 1283.0 HRMS Calcd for $C_{32}H_{44}N_3O_2$: 502.3434 $[M + H]^+$, found: 502.3427; $[\alpha]_D^{18}$ = + 63.96 (*c* 1.0, $CHCl_3$).

2.5.8. General procedure for synthesis of bis(oxazoline) carbazole ligand 2.4 from 1,8-dihalocarbazole 2.17 via Pd–catalyzed carbonylative amidation followed by BF_3•OEt_2 induced cyclization

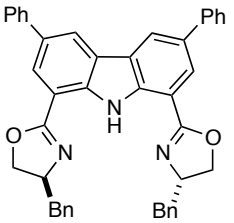
A modified procedure reported by Nakada *et al* was used.[50] To a solution of 0.5 mmol of the 1,8-diiodocarbazole and $Pd(PPh_3)_4$ (20 mol%) in 5 mL of dry, degassed DMF was added the corresponding amino alcohol (2.6 equiv) and Et_3N (4 equiv) via a syringe. CO gas was then bubbled through the reaction mixture and a balloon of CO placed over the reaction flask. The reaction mixture was stirred at 60 °C for 8 h. After the mixture was cooled down it was diluted with CH_2Cl_2, washed with brine and 1 M $CuSO_4$ several times. The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure to give the desired bisamide **2.19**. The bisamide was partially purified by passing through a short silica bed and eluting with CH_2Cl_2 and methanol. The eluent was concentrated under reduced pressure and the bisamide thus obtained was suspended in 15% w/v of BF_3•Et_2O. The resulting suspension was stirred at 120 °C for 6 h. The red mixture was cooled to room temperature and poured into ice cold 2 M NaOH (5 mL), extracted with CH_2Cl_2, washed with a saturated solution of $NaHCO_3$, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography to afford the desired ligand.



(4*S*,4'*S*)-2,2'-(3,6-diphenyl-9*H*-carbazole-1,8-diyl)bis(4-isopropyl-4,5-dihydrooxazole)[47b]**:** Purification by flash chromatography (20%-50% CH_2Cl_2 in hexanes) afforded the product as a yellow solid (430 mg, 0.79 mmol, 57%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.48 (d, *J* = 1.44 Hz, 2 H), 8.21(d, *J* = 1.69 Hz, 2 H), 7.77 (d, *J* = 7.80 H, 4 H), 7.53-7.46 (m, 4H), 7.37 (app t, *J* = 7.30 Hz, 2H), 4.58-4.46 (m, 2H), 4.33-4.20 (m, 4H), 1.94 (oct, *J* = 6.58 Hz, 2H), 1.19 (d, *J* = 6.69 Hz, 6 H), 1.06 (d, *J* = 6.69 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 141.4, 138.8, 132.4, 128.8, 127.3, 126.7, 125.2, 124.2, 121.8, 110.8, 72.9, 69.9, 33.4, 19.6, 18.6.

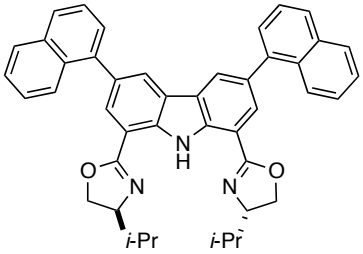


(4R,4'R)-2,2'-(3,6-diphenyl-9H-carbazole-1,8-diyl)bis(4-phenyl-4,5-dihydrooxazole) (2.4d): Purification by flash chromatography (50% CH_2Cl_2 in hexanes) afforded the product as a bright yellow solid (164 mg, 0.27 mmol, 27%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 11.91 (s br, 1 H), 8.51 (d, *J* = 1.23, 2 H), 8.29 (d, *J* = 1.67, 2 H), 7.8 (d, *J* = 8.7, 4 H), 7.53 (d, *J* = 7.4, 4 H), 7.45-7.28 (m, 12 H), 5.55 (t, *J* = 9.43 2 H), 4.90 (dd, *J* = 8.52, 9.17, 2 H), 4.36 (t, *J* = 8.70 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.9, 142.6, 141.5, 139.1, 132.7, 129.1, 128.8, 127.5, 127.0, 126.9, 125.5, 124.5, 122.4, 110.7, 74.0, 70.1; IR (thin film) 3354.1, 3059.6, 2962.4, 1949.1, 1719.0. 1645.8, 1478.8; HRMS (MALDI) calcd for $C_{42}H_{31}N_3O_2$ (M + H) 609.2416 found 609.9933 $[\alpha]_D^{18}$ = –135.6 (*c* 1.0, $CHCl_3$).

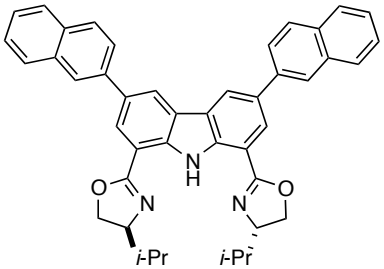


(4*S*,4'*S*)-2,2'-(3,6-diphenyl-9*H*-carbazole-1,8-diyl)bis(4-benzyl-4,5-dihydrooxazole) (2.4e): Purification by flash chromatography (50% CH_2Cl_2 in hexanes) affords the product as a bright yellow solid (159 mg, 0.25 mmol, 25%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 11.91 (s br, 1 H), 8.41

(d, *J* = 1.84 Hz, 2 H), 8.12 (d, *J* = 1.67 Hz, 2 H), 7.68 (d, *J* = 8.0 Hz, 4 H), 7.41 (d, *J* = 7.1 Hz, 4 H), 7.25 (m, 12 H), 4.7 (quint, *J* = 7.51 Hz, 2 H), 4.55-4.33 (m, 6 H), 4.12 (app t, *J* = 8.0 Hz, 2 H), 3.22 (dd, *J* = 5.5, 13.79 Hz, 2 H), 2.82 (dd, *J* = 8.32, 13.7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.0, 141.3, 138.8, 138.0, 132.5, 129.4, 128.8, 128.5, 127.3, 126.7, 126.4, 125.3, 124.2, 122.0, 110.7, 71.3, 67.8, 42.0; IR (thin film) 3345.1, 2897.0, 1646.3, 1619.8, 1478.3, 1265.6; HRMS (MALDI) calcd for $C_{44}H_{35}N_3O_2$ (M + H) 638.2802, found 638.2807 $[\alpha]_D^{18}$ = + 51.34 (*c* 1.0, $CHCl_3$).



(4S,4'S)-2,2'-(3,6-di(naphthalen-1-yl)-9H-carbazole-1,8-diyl)bis(4-isopropyl-4,5-dihydrooxazole) (2.4g): Purification by flash chromatography (4:1 hexanes/CH_2Cl_2) afforded 35% of the product as a yellow solid. mp 139-141 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.06 (d, *J* = 6.3 Hz, 6H), 1.20 (d, *J* = 6.6 Hz, 6H), 1.91-1.95 (m, 2H), 4.18-4.29 (m, 4H), 4.47-4.52 (m, 2H), 7.39-7.55 (m, 8H), 7.85-7.97 (m, 6H), 8.10 (d, *J* = 1.5 Hz, 2H), 8.31 (d, *J* = 1.5 Hz, 2H), 12.20 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 18.9, 19.4, 33.7, 70.1, 73.1, 110.6, 123.7, 125.0, 125.5, 125.9, 126.2, 126.3, 127.6, 127.7, 128.1, 128.4, 131.7, 132.3, 134.0, 138.9, 140.4, 162.6; IR 3429.6, 1719.3, 1508.4; HRMS Calcd for $C_{44}H_{40}N_3O_2$: 642.3114 $[M + H]^+$, found: 642.3123; $[\alpha]_D^{18}$ = + 30.01 (*c* 1.0, $CHCl_3$).

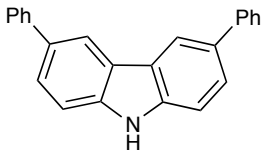


(4S,4'S)-2,2'-(3,6-di(naphthalen-2-yl)-9H-carbazole-1,8-diyl)bis(4-isopropyl-4,5-dihydrooxazole) (2.4h): Prepared by a modification of previously reported procedures[50]. Compound **2.16c** (470 mg, 1.12 mmol) was suspended in a mixture of AcOH, H_2O and H_2SO_4 (1: 0.2: 0.03). After addition of I_2 (142 mg, 1.12 mmol) and

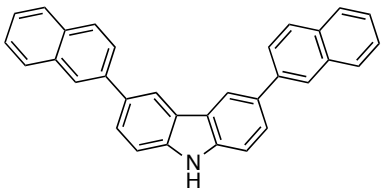
$HIO_4 \cdot 2H_2O$ (127 mg, 0.56 mmol), the pink suspension was stirred at 80 °C for 5 hours. The mixture was then cooled down to r.t. and poured into water. The solid was filtrated and dried under reduced pressure (600 mg, 0.89 mmol, 80% crude yield). After recrystallization from toluene pure 1,8-diiodo-3,6-di(naphthalen-2-yl)-9*H*-carbazole was obtained as a pink solid (130 mg, 0.2 mmol, 18% yield. Next, the procedure described above for the synthesis of bis-oxazoline carbazoles was followed**.** Purification by flash chromatography (50 to 80% CH_2Cl_2 in hexanes) afforded the title compound as a yellow solid, more than 90% pure (32 mg, 0.05 mmol, 25% yield). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.65 (s, 2 H), 8.35 (m, 2 H), 8.22 (m, 2 H), 7.99-7.88 (m, 8 H), 7.58-7.46 (m, 4 H), 4.54 (m, 2 H), 4.28 (m, 4 H), 1.95 (m, 2 H), 1.22 (d, *J* = 6.17 Hz, 6 H), 1.08 (d, *J* = 6.36 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4, 138.9, 138.7, 133.8, 132.37, 132.33, 128.4, 128.1, 127.6, 126.2, 125.9, 125.7, 125.6, 125.5, 124.3, 122.1, 110.9, 72.9, 70.0, 33.4, 19.2, 18.6; IR (thin film) 3052.9, 2958.6, 1649.14, 1601.4, 1486.1, 14363.7; MS (APCI) calcd for $C_{44}H_{35}N_3O_2$ (M + H) 642.31, found 642.54. $[\alpha]_D^{18}$ = + 55.6 (*c* 1.0, $CHCl_3$).

2.5.9 Representative procedure for the synthesis of carbazoles 2.16

Prepared by modification of the procedure reported by Nakada *et al*[47b] 3,6 diiodocarbazole **2.14** (2 g, 4.84 mmol), boronic acid **2.15** (14.5 mmol) and $Ba(OH)_2 \cdot 8H_2O$ (4.5 g, 14.5 mmol) weere dissolved in a 6:1 mixture of DME/H_2O (60 mL). A solution of $Pd(OAc)_2$ (54.3 mg, 0.24 mmol) and P(*o*-tol)$_3$ (148 mg, 0.48 mmol) in DME (5mL) was then added *via* cannula. The mixture was stirred at 80 °C for 18 h and then cooled to rt. The precipitate was removed by filtration and the filtrate was extracted with CH_2Cl_2. The organic phase was dried over Mg_2SO_4 and concentrated under reduced pressure.

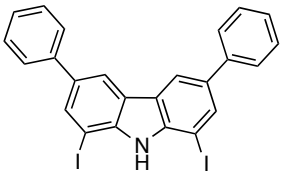


3,6-diphenyl-9*H*-carbazole (2.16a)[47b]**:** Purified by column chromatography (25% CH_2Cl_2 in hexanes) to give a white solid (4.1 g, 12.8 mmol, 65%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.36 (d, *J* = 2.90, 2 H), 8.14 (s, 1 H), 7.73 (m, 4 H), 7.70 (d, *J* = 1.82 Hz, 2 H), 7.54 (d, *J* =0.52 Hz, 2 H), 7.52-7.46 (m, 4 H), 7.36 (tt, *J* =1.20, 6.60 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.0, 139.4, 133.2, 128.8, 127.3, 126.3, 125.6, 124.0, 118.9, 110.9.



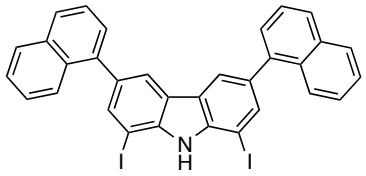
3,6-di(naphthalen-2-yl)-9H-carbazole (2.16c): Purified by column chromatography (30% CH_2Cl_2 in hexanes) and then recrystallized from toluene. The product was obtained in 23% yield as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.53 (s, 2 H), 8.19 (s, 3 H), 8.01-7.83 (m, 10 H), 7.61-7.47 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.7, 139.5, 134.1, 133.2, 132.5, 128.6, 128.3, 127.9, 126.4, 126.3, 126.1, 125.9, 125.8, 124.3, 119.5, 111.3; HRMS (MALDI) calcd for $C_{32}H_{22}N$ (M^+H) 420.1752, found 420.5908.

2.5.10 Synthesis of di-iodocarbazoles 2.17



1,8-diiodo-3,6-diphenyl-9*H*-carbazole (2.17a)[47b]**:** Carbazole **2.17a** (2.37 g, 7.42 mmol) was suspended in a mixture of AcOH, H_2O and H_2SO_4 (1: 0.2: 0.03). After addition of I_2 (0.94 g, 7.42 mmol) and $HIO_4{\cdot}2H_2O$ (0.85 g, 3.71 mmol), the pink suspension was stirred at 80 °C for 5 hours. The mixture was then cooled down to r.t. and poured into water. The solid was filtrated and washed with a saturated solution of NaS_2O_3, $NaHCO_3$ and brine. After recrystallization from toluene the pure compound was obtained as a pink solid (1.42 g, 2.5 mmol, 34%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.23 (d, *J* = 1.22 Hz, 2 H), 8.16 (s, 1H), 8.07 (d, *J* = 1.47 Hz, 2H), 7.67 (d, *J* = 7.50 Hz,

4H), 7.52-7.45 (m 4 H), 7.38 (tt, *J* = 1.33, 3.79 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.4, 140.3, 135.6, 134.4, 128.9, 127.3, 127.1, 124.6, 119.4, 76.4.



1,8-diiodo-3,6-di(naphthalen-1-yl)-9H-carbazole (2.17b)[50, 80]: $BnMe_3NCl_2I$ was added to a suspension of **2.16b** in a mixture of AcOH (33 mL) and H_2SO_4 (1 mL). The mixture was stirred at 60 °C until the reaction was completed as judged by TLC. The mixture was cooled to rt and poured into 60 mL of water. The precipitate was filtered and partitioned between EtOAc (33 mL) and a saturated solution of $NaHCO_3$ (10 mL). The organic layer was washed with a saturated solution of $Na_2S_2O_3$ (20 mL) and brine (40 mL), dried over Na_2SO_4 and concentrated under reduced pressure. Flash chromatography (ethyl acetate:hexanes, 1:50) afforded title compound, more than 90% pure, in 40% yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.32 (s, 1H), 8.11 (s, 2H), 7.99 (d, *J* = 1.39 Hz, 2H), 7.94-7.85 (m, 7H), 7.57-7.40 (m, 7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.3, 139.0, 136.9, 136.8, 134.7, 133.7, 131.8, 128.3, 127.8, 127.4, 127.1, 126.2, 125.8, 125.3, 124.0, 122.3; IR 3429.9, 3054.3, 2924.4, 1722.1, 1508.4 HRMS (MALDI) calcd for $C_{32}H_{19}I_2N$ (M - I) 544.0557, found 544.2573.

2.5.11 Preparation of 3-methyl-1-phenyl-4-((trimethylsilyl)methyl)hexa-4,5-dien-3-ol (2.33a) under acidic conditions

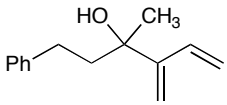
Inside a nitrogen atmosphere drybox, a mixture of $CrCl_3$ (17 mg, 0.1 mmol, 0.3 equiv), Mn powder 325-mesh (40 mg, 0.7 mmol, 2 equiv) were added to a 2-dram vial. Then, the vial was capped with a teflon lid and it was removed from the drybox. Dry THF (2.5 mL) was added by syringe and a suspension was formed. Then, TMSCl (93 μL, 0.7 mmol, 2 equiv) and Et_3N (50 μL, 0.3 mmol, 1 equiv) were added by syringe. The mixture is allowed to stir 20 minutes and (4-

bromo-2-butyn-1-yl)trimethylsilane (222 mg, 1 mmol, 3 equiv) is added. After 30 min, the ketone (0.36 mmol, 1 equiv) is added and the mixture is stirred for 24 hours. 1 M HCl was added and the obtained green solution was stirred until the alcohol is completely deprotected as judged by TLC. A saturated solution of NH_4Cl (2 mL) was added and the mixture was extracted with three portions of ethyl acetate. The combined organic fractions were washed with brine, dried over Mg_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography or preparative thin layer chromatography (10% EtOAc in hexanes as eluent) and was obtained as a clear oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.23-7.17 (m, 2 H), 7.21-7.15 (m, 3 H), 4.38 (t, *J* = 3.59 Hz, 2H), 2.65-2.44 (m, 2 H), 1.94-1.78 (m, 2 H), 1.74 (s, 1 H), 1.33-1.24 (dt, *J* = 3.51, 15.6 Hz, 1 H), 1.27 (s, 3 H), 1.23-1.15 24 (dt, *J* = 3.30, 15.62 Hz, 1 H), 0.0 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 142.5, 128.3, 128.3, 125.6, 107.5, 79.4, 27.9, 42.2, 30.4, 27.1, 15.2, -0.8; IR (thin film) 3454.3, 3085.6, 2952.4, 1949.05, 1603.7, 1496.6 HRMS (ESI) calcd for $C_{17}H_{17}OSi$ (M + H) 275.1831 found 275.1753.

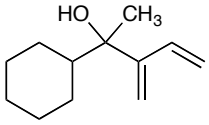
2.5.12 General method for the preparation of tertiary 1,3-butadien-2-ylcarbinols (2.41)

Inside a nitrogen atmosphere drybox, a mixture of $CrCl_3$ (17 mg, 0.1 mmol, 0.3 equiv), Mn powder 325-mesh (40 mg, 0.7 mmol, 2 equiv) were added to a 2-dram vial. Then, the vial was capped with a teflon lid and it was removed from the drybox. Dry THF (2.5 mL) was added by syringe and a suspension was formed. Then, TMSCl (93 μL, 0.7 mmol, 2 equiv) and Et_3N (50 μL, 0.3 mmol, 1 equiv) were added by syringe. The mixture is allowed to stir 20 minutes and (4-bromo-2-butyn-1-yl)trimethylsilane (222 mg, 1 mmol, 3 equiv) is added. After 30 min, the ketone (0.36 mmol, 1 equv) is added and the mixture is stirred for 24 hours. After this time the suspension is filtered through a path of silica gel and rinsed with ether. The solvent is removed and the residue is redisolved in THF (1 mL). TBAF (2.88 mL of a 1 M solution, 2.88 mmol, 8

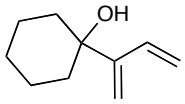
equiv) is added and the solution is stirred for 20 hours or until the reaction is completed as judged by TLC. A saturated solution of NH_4Cl (2 mL) was added and the mixture was extracted with three portions of ethyl acetate. The combined organic fractions were washed with brine, dried over Mg_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography or preparative thin layer chromatography.



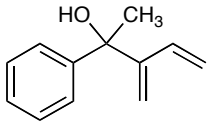
3-methyl-4-methylene-1-phenylhex-5-en-3-ol (2.41a): Obtained as a clear yellow oil (25 mg, 0.12 mmol, 69%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.31-7.25 (m, 2 H), 7.21-7.15 (m, 3 H), 6.38 (dd, *J* = 10.9, 17.0 Hz, 1 H), 5.54 (dd, *J* = 1.84, 17.12 Hz, 1 H), 5.35 (s, 1 H), 5.17 (d, *J* = 1.35 Hz, 1 H), 5.44 (dd, *J* = 1.97, 10.93 Hz, 1 H), 2.96-2.49 (m, 2 H), 1.94 (d, *J* = 8.83 Hz, 1 H), 1.92 (d, *J* = 10.2 Hz, 1 H), 1.56 (s br, 1 H), 1.42 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7, 142.3, 135.4, 128.3, 128.3, 125.7, 115.9, 110.0, 74.6, 42.8, 30.1, 28.2; IR (thin film) 3452.5, 3085.1, 2931.7, 1603.7 HRMS (ESI) calcd for $C_{14}H_{18}O$ (M + Li) 209.1518, found 209.1577.



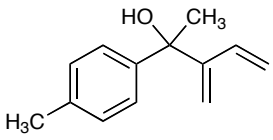
2-cyclohexyl-3-methylenepent-4-en-2-ol (2.41b): Obtained as a tan oil (26 mg, 0.14 mmol, 41%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.27 (dd, *J* = 10.5, 16.5 Hz, 1 H), 5.39 (dd, *J* = 2.1, 17.4 Hz, 1 H), 5.16 (t, *J* = 1.31 Hz, 1 H), 4.99 (dd, *J* = 2.9, 11.0 Hz, 1H), 4.66 (dd, *J* = 1.66, 4.96 Hz, 1H), 1.76-1.58 (m, 5 H), 1.42-1.30 (m, 2H), 1.23 (s, 3 H), 1.12-0.92 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.4, 135.7, 115.5, 109.5, 76.5, 44.9, 26.7, 26.6, 26.4, 24.6 IR (thin film) 3462.4, 2929.8, 2852.9, 1450.4, 1372.5 cm^{-1}; GC/MS calcd for $C_{12}H_{20}O$ (M) 181.1: found 181.1.



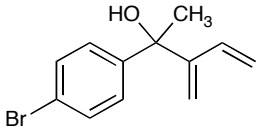
1-(buta-1,3-dien-2-yl)cyclohexanol (2.41c)[58]: Obtained as clear oil (9 mg, 0.06 mmol, 23%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.31 (dd, *J* = 11.9, 18.4 Hz, 1 H), 5.46 (dd, *J* = 2.24, 17.45 Hz, 1 H), 5.14 (d, *J* = 1.37 Hz, 1 H), 5.08 (d, *J* = 1.38 Hz, 1H), 5.08 (dd, *J* = 1.51, 11.18 Hz, 1H), 1.9-1.60 (m, 10 H). 1.31 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.7, 135.9, 115.7, 109.9, 83.7, 39.1, 23.7, 23.7; IR (thin film) 3386.3, 2960.6, 2873.2, 1630.1, 1422.4, 1377.2 cm^{-1}; GC/MS calcd for $C_{10}H_{16}O$ (M) 152.1, found 152.1.



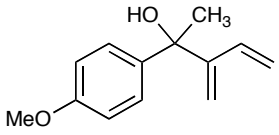
3-methylene-2-phenylpent-4-en-2-ol (2.41d)[81]: Obtained as a clear oil (28.5 mg, 0.16 mmol, 45%).^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.48-7.43 (m, 2 H), 7.37-7.23 (m, 3 H), 6.11 (dd, *J* = 11.4, 17.72 Hz, 1 H), 5.37 (d, *J* = 9.85 Hz, 2 H), 5.28 (dd, *J* = 1.69, 17.66 Hz, 1 H), 5.00 (dd, *J* = 1.53, 11.08 Hz, 1 H), 2.04 (s, 1 H), 1.71 (s, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.7, 146.0, 135.4, 128.2, 126.9, 125.2, 116.5, 112.0, 76.0, 29.5; IR (thin film) 3449.7, 3086.2, 2979.80 1632.0; HRMS (ESI) calcd for $C_{12}H_{14}O$ (M+Li) 181.1205, found 181.1197.



3-methylene-2-*p*-tolylpent-4-en-2-ol (2.41e): Obtained as a clear oil (35 mg, 0.18 mmol, 53%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.37 (d, *J* = 8.27 Hz, 2 H), 7.17 (d, *J* = 8.27 Hz, 2 H), 6.16 (dd, *J* = 11.11, 17.38 Hz, 1 H), 5.39 (d, *J* = 9.05 Hz, 2 H), 5.32 (dd, *J* = 1.63, 17.58 Hz, 1 H), 5.03 (dd, *J* = 1.68, 11.23 Hz, 1 H), 2.37 (s, 3 H), 2.02 (s, 1 H), 1.72 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.9, 143.1, 136.6, 135.5, 128.9, 125.2, 116.4, 111.7, 75.9, 29.4, 21.0; IR (thin film) 3450, 2979, 2924, 1955, 1610 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{16}O$ (M+Li) 195.1361, found 195.1367.



2-(4-bromophenyl)-3-methylenepent-4-en-2-ol (2.41f): Obtained as a clear oil (59 mg, 0.23 mmol, 67%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.37 (d, *J* = 8.6, Hz, 2 H), 7.25 (d, *J* = 8.6 Hz, 1 H), 6.02 (dd, *J* = 11.4, 17.8 Hz, 1H), 5.32 (s, 1 H), 5.27 (s, 1 H), 5.20 (dd, *J* = 1.47, 17.42 Hz, 1 H), 4.95 (dd, *J* = 1.38, 11.15 Hz, 1 H), 1.95 (s, 1 H), 1.60(s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.1, 145.2, 135.1, 131.2, 127.1, 120.9, 117.0, 112.6, 75.8, 29.7 IR (thin film) cm^{-1}; MS (APCI) calcd for $C_{12}H_{13}BrO$ (M+Li) 251.0072, found 251.0071.



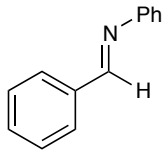
2-(4-methoxyphenyl)-3-methylenepent-4-en-2-ol (2.41g)[81]**:** Obtained as a clear oil (29 mg, 0.14 mmol, 51%).^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.36 (d, *J* = 9.42 Hz, 2 H), 6.86 (d, *J* = 9.42 Hz, 2 H) 6.11 (dd, *J* = 11.35, 17.49 Hz, 1 H), 5.37 (s, 1 H), 5.35 (s, 1 H), 5.29 (d, *J* = 1.52, 17.4 Hz, 1 H), 5.01 (dd, *J* = 1.71, 17.4 Hz, 1 H), 3.80 (s, 3 H), 1.99 (s, 1 H), 1.69 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 152.1, 138.1, 135.5, 126.5, 116.3, 113.5, 111.6, 75.7, 55.2, 19.3; IR (thin film) 3473, 2977, 2934, 2836, 1955, 1610, 1510cm^{-1}; MS (ESI) calcd for $C_{13}H_{16}O_2$ (M-OH) 187.1117: found 187.1119.

Preparation of 3-methylene-2-phenylpent-4-en-2-ol (3d)[81] **using ligand 2.4b**

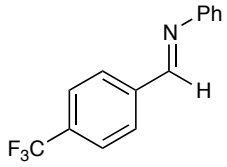
Inside a Nitrogen atmosphere drybox, $CrCl_3$ (1.5 mg, 0.01 mmol), **2.4b**[47b] (6 mg, 0.01 mmol) and Mn^0 powder 325-mesh (22 mg, 0.4 mmol) were added to a 2-dram vial. Then, the vial was capped with a Teflon lid and it was removed from the drybox. Dry THF (2 mL) was added via syringe and a gray suspension was formed. This was followed by addition of (4-bromo-2-butyn-1-yl)trimethylsilane **2.5** (50 mg, 0.24 mmol). After 30 min, the mixture was cooled to 0 °C and acetophenone (23 μL, 0.2 mmol) followed by TMSCl (30 μL, 0.22 mmol)

were added. The mixture was stirred at room temperature for 18 h, 1 M HCl was added (1 mL) and was extracted with three portions of diethyl ether. The mixed organic phases were washed with brine, dried with Mg_2SO_4 and concentrated under reduced pressure. The residue was redissolved in THF (1.5 mL) and 1 M TBAF (1.5 mL) was added. When the reaction was completed, as judged by TLC, a saturated solution of NH_4Cl (3 mL) was added and the mixture was extracted with three portions of EtOAc. The combined organic fractions were washed with brine, dried over Mg_2SO_4 and concentrated under reduced pressure. Enantiomeric excess determined by HPLC (250 nm) using a ChiralPAK AS-H column (hexanes : isopropanol = 98:2, flow rate = 0.6 mL/min) retention time: = 10.7 min, 11.5 min.

2.5.13 Preparation of imines

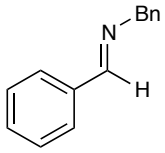


***N*-benzylideneaniline (2.58a)[82]:** Prepared following the procedure described for the synthesis of compound **2.59**. Product obtained as a light yellow solid (3 g, 16.5 mmol, 60%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.50 (s, 1 H), 7.99 (m, 2 H), 7.55-7.49 (m, 3 H), 7.47-7.40 (m, 2 H), 7.28-7.22 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 160.4, 152.0, 136.2, 131.3, 129.1, 128.8, 128.7, 125.9, 120.8.

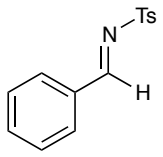


(4-bromobut-2-yn-1-yl)trimethylsilane (2.58b)[83]: *p*-(trifluoromethyl)benzaldehyde (1.36 mL, 10 mmol) and aniline (0.8 mL, 9 mmol) were dissolved in Toluene (100 mL) and stirred under reflux for 16 h. The solution was cooled to r.t. and toluene was removed under reduced pressure. After recrystallization from hexanes the product was obtained as a white solid. (1.93 g, 7.75 mmol, 77%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.54 (s, 1H), 8.06 (d, *J* = 8.04 Hz, 2 H), 7.77 (d, *J* = 8.21

Hz, 2 H), 7.49-7.41 (m, 2 H), 7.34-7.29 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 158.5, 129.2, 128.9, 126.5, 125.6 (q, J = 4.3), 120.8.



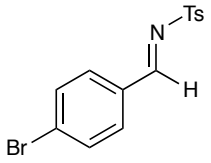
(4-bromobut-2-yn-1-yl)trimethylsilane (2.59)[84]**:** A mixture of benzaldehyde (2.6 mL, 25.6 mmol), benzylamine (2.8 mL, 25.6 mmol) and $MgSO_4$ (7 g) in 25 mL of benzene was stirred at r.t. for 24 h. After this time, $MgSO_4$ was removed by filtration and rinsed with CH_2Cl_2. The solution was then concentrated under reduced pressure to give a yellow oil. The residue was distilled under reduced pressure (105-120 °C at 320 mTorr) to afford a clear oil (2.6 g, 13.3 mmol, 51 %). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.44 (t, J = 1.42 Hz, 1 H), 7.85-8.81 (m, 2 H), 7.49-7.44 (m, 3 H), 7.40-7.38 (m, 4 H), 7.32 (m, 1 H), 4.87 (d, J = 1.37 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) 162.0, 139.2, 136.1, 130.7, 128.6, 128.4, 128.2, 127.9, 126.9, 65.0.



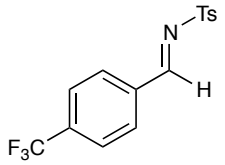
***N*-benzylidene-4-methylbenzenesulfonamide (2.60a)**[85]**:** Following the procedure reported by Wynne *et al*. *p*-toluenesulfonamide (4.5 g, 26.28 mmol) was mixed with dry toluene (70 mL). Next, benzaldehyde (2.4 mL, 26.28 mmol) was added via syringe and the mixture was heated to reflux with a Dean-Stark trap for 24 h or until completion of the reaction as judged by H^1 NMR. After the solution was cooled down, toluene was removed under reduced pressure to afford a white solid. The compound was recrystallized from diethyl ether to afford the pure imine as white (6.16 g, 23.7 mmol, 90%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.02 (s, 1 H), 7.91 (m, 4 H), 7.6 (t, J = 7.05 Hz, 1 H), 7.48 (t, J = 7.56 Hz, 2 H), 7.34 (d, J = 8.33 Hz, 2H), 2.43 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.1, 144.5, 134.4, 132.3, 131.2, 129.7, 129.1, 128.0, 126.2, 21.6.

2.5.14 General method for the preparation of N-tosyl imines

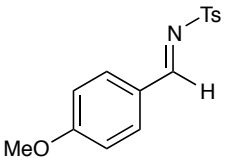
Following a modification of the procedure reported by Duguet[86] *et al*. *p*-toluenesulfonamide (1.4 g, 7.78 mmol) was mixed with dry toluene (70 mL). Next aldehyde (7.78 mmol) and $BF_3{\cdot}OEt_2$ (300 μl) were sequentially added to the reaction mixture via syringe. Mixture was heated to reflux with a Dean-Stark trap for 24 h or until completion of the reaction as judged by H^1 NMR. After the solution was cooled down, ethyl acetate was added to completely dissolve the newly formed precipitate (if any). The solution was washed with 1 M NaOH and brine. The organic phase was dried over Mg_2SO_4 and concentrated under reduced pressure. The solid was recrystallized from a mixture of ethyl acetate and hexanes to afford the pure imine.



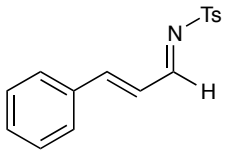
***N*-(4-bromobenzylidene)-4-methylbenzenesulfonamide (2.60b)[86]:** Obtained as a white solid (1.4 g, 4.18 mmol, 53%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.98 (s, 1H), 7.89 (d, *J* = 8.66 Hz, 2H), 7.79 (d, *J* = 8.66 Hz, 2H), 7.65 (d, *J* = 8.28 Hz, 2H), 7.65 (d, *J* = 8.47 Hz, 2H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 144.8, 134.8, 132.5, 132.3, 131.2, 130.2, 129.8, 128.1, 21.6.



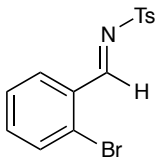
4-methyl-*N*-(4-(trifluoromethyl)benzylidene)benzenesulfonamide (2.60c)[87]: Obtained as a white solid (1.95 g, 5.9 mmol, 31%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.1 (s, 1H), 8.06 (d, *J* = 8.5 Hz, 2H), 7.91 (d, *J* = 8.23 Hz, 2H), 7.76 (d, *J* = 8.53 Hz, 2H), 7.38 (d, *J* = 7.9 Hz, 2H), 2.4 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 145.1, 134.4, 131.3, 129.9, 128.3, 126.2 (q, *J* = 3.9), 19.4; MS (ESI) calcd for $C_{15}H_{12}F_3NO_2S$ 237.0541, found 237.9835.



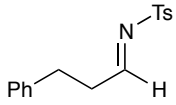
***N*-(4-methoxybenzylidene)-4-methylbenzenesulfonamide (2.60d)[88]:** Obtained as white crystals (4.1 g, 14 mmol, 85%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.95 (s, 1 H), 7.9 (d , *J* = 8.1 Hz, 2H), 7.8 (d, *J* = 8.4 Hz, 2 H), 7.34 (d, *J* = 8.21 Hz, 2 H), 6.78 (d, *J* = 9.1 Hz, 2 H), 3.9 (s, 3 H), 2.4 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.2, 165.2, 144.5, 135.8, 133.7, 129.7, 127.9, 125.2, 114.6, 55.6, 21.7; HRMS (ESI) calcd for $C_{15}H_{15}NO_3S$ (M + H) 290.0851, found 290.0860.



4-methyl-*N*-((*E*)-3-phenylallylidene)benzenesulfonamide (2.60e)[86]: Obtained as light brown crystals (0.83 g, 1.33, 25%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.78 (d, *J* = 9.42 Hz, 1H), 7.86 (d, *J* = 8.8 Hz, 2H), 7.58-7.51 (m, 2 H), 7.47-7.41 (m, 4 H), 7.34 (d, *J* = 8.0 Hz, 2H) 6.99 (dd, *J* = 9.36, 15.81 Hz, 2H), 2.43 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9, 153.8, 144.5, 135.3, 134.1, 131.7, 129.8, 129.2, 128.6, 128.0, 124.7, 21.7; HRMS (ESI) calcd for $C_{16}H_{15}NO_2S$ (M + H) 286.0902, found 286.0913.

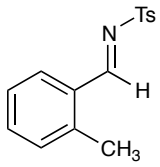


***N*-(2-bromobenzylidene)-4-methylbenzenesulfonamide (2.60h)[89]**: Obtained as a white needles (1.4 g, 4.15 mmol, 81%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.43 (s, 1 H), 8.14 (dd, *J* = 2.03, 7.52 Hz, 1H), 7.90 (d, *J* = 8.51 Hz, 2 H), 7.65 (dd, *J* = 1.38, 7.74 Hz, 1 H), 7.47-7.44 (m, 4 H), 2.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.1, 144.8, 135.7, 134.6, 133.7, 131.1, 130.6, 129.8, 128.8, 128.3, 127.9, 21.6; HRMS (ESI) calcd for $C_{14}H_{12}BrNO_2S$ 337.9850 found 337.9853.



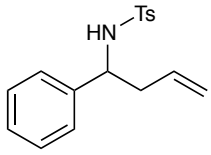
4-methyl-*N*-(3-phenylpropylidene)benzenesulfonamide (2.60f)[90]: Prepared following the procedure describer for the preparation of compound **2.60g** as

previously described by Wipf.[90] Obtained as a white solid after recrystallization from hexanes (1.4 g, 4.9 mmol, 49%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.62 (t, *J* = 4.06 Hz, 1 H), 7.77 (d, *J* = 8.53 Hz, 2H), 7.33 (*J* = 8.13 Hz, 2H), 7.28-7.10 (m, 5 H), 2.98-2.92 (m, 2 H), 2.88-2.80 (m, 2 H), 2.4 (s, 3 H); 177.4, 144.7, 139.6, 134.3, 129.8, 128.6, 128.3, 128.1, 126.4, 37.3, 30.6, 21.6; IR (thin film) 2924.9, 1628.6, 1453.4, 1089.6 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{17}NO_2S$ (M + Li) 294.1140, found 294.1127.



4-methyl-*N*-(2-methylbenzylidene)benzenesulfonamide (2.60g)[91]: Prepared following the procedure described by Chemla *et al*.[71] Sodium *p*-toluenesulfinate -methylbenzaldehyde (1.15 mL, 10 mmol) were dissolved in a 1:1 solution of formic acid/H_2O (30 mL). The mixture was stirred at r.t. for 1 week until the aldehyde was consumed as judged by TLC. After this time, the white precipitate was collected by filtration and rinsed with water and hexanes. The white solid was dissolved in CH_2Cl_2 (50 mL), a saturated solution of $NaHCO_3$ (50 mL) was added and the mixture was stirred for 2 h. The aqueous layer was extracted with CH_2Cl_2. The combined organic phases were washed with brine dried over $MgSO_4$ and concentrated under reduced pressure. The desired imine was obtained as a white solid and was used without further purification (2.02 g, 7.4 mmol, 74%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 9.95 (s, 1 H), 7.9 (d, *J* = 8.1 Hz, 2H), 7.8 (d, *J* = 8.4 Hz, 2 H), 7.34 (d, *J* = 8.21 Hz, 2 H), 6.78 (d, *J* = 9.1 Hz, 2 H), 3.9 (s, 3 H), 2.4 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.6, 144.4, 142.2, 135.4, 134.5, 131.4, 130.46 130.4, 129.7, 128.0, 126.5, 21.5, 19.6.

2.5.15 4-methyl-N-(1-phenylbut-3-en-1-yl)benzenesulfonamide (2.62)[67]

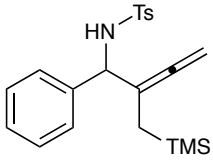


Inside a Nitrogen atmosphene Drybox, a mixture of $CrCl_3$ (4.5 mg, 0.03 mmol) and Mn powder 325-mesh (33mg, 0.66 mmol) were added to a 2-dram vial. The vial was capped with a Teflon lid and it was removed from the drybox. Tosylimine **2.60a** (77mg, 0.3 mmol) was added to the mixture and the vial was flushed with argon. Dry THF (2 mL) was added via syringe and a brown suspension was formed. This was followed by addition of TMSCl (42 μl, 0.33 mmol) and freshly distilled allyl bromide (40 μl, 0.45 mmol). The mixture was stirred at room temperature for 16 h. ethyl acetate (1 -2 mL) was added to the gray suspension and the mixture was filtered trough a path of silica to remove solids. The resulting clear solution was concentrated under reduced pressure and the residue was redisolved in THF (3 mL). TBAF (1 M in THF, 0.3 mL, 0.3 mmol) was added and the mixture was stirred for 10 min. A saturated solution of NH_4Cl was added and the mixture was extracted with ethyl acetate. The organic phases were dried over Mg_2SO_4, filtered though a path of silica and concentrated under reduced pressure. The residue was purified by flash chromatography using a gradient of ethyl acetate in hexanes (15 to 20%) to afford the desired product as a clear oil (80 mg, 0.27 mmol, 88%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.57 (d, *J* = 7.57 Hz, 2 H), 7.20-7.05 (m, 7 H), 5.51 (m, 1 H), 5.23 (d, *J* = 6.98 Hz, 1 H), 5.13 (m, 2 H), 4.46 (q, *J* = 6.84 Hz, 1H), 2.46 (q, *J* = 6.24 Hz, 2 H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.0, 140.3, 137.5, 133.1, 129.2, 128.3, 127.3, 127.1, 126.5, 119.1, 57.2, 41.8, 21.4.

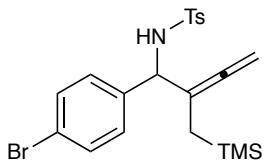
2.5.16 General Method for the preparation of (silylmethyl)allenic amines

Inside a Nitrogen atmosphene Drybox, a mixture of $CrCl_2$ (11 mg, 0.09 mmol) and Mn powder 325-mesh (33mg, 0.66 mmol) were added to a 2-dram vial. The vial was capped with a Teflon lid and it was removed from the drybox. The tosylimine (0.3 mmol) was added to the

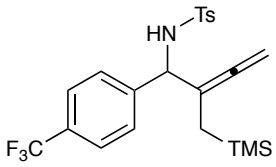
mixture and the vial was flushed with argon. Dry THF (2 mL) was added via syringe and a brown suspension was formed. This was followed by addition of TMSCl (42 μl, 0.33 mmol) and (4-bromo-2-butyn-1-yl)trimethyl-silane (120 mg, 0.6 mmol). The mixture was stirred at room temperature for 48 h. Et_3N (1 mL) and ethyl acetate (1 -2 mL) were added to the gray suspension and the brown mixture was filtered trough a path of silica using ethyl acetate as eluent. The resulting clear solution was concentrated under reduced pressure and the residue was redisolved in THF (3 mL). TBAF (1 M in THF, 0.45 mL, 0.45 mmol) was added to the solution in two parts over 10 minutes. The mixture was stirred for a maximum of 30 min or until the majority of propargylamine is consumed to afford the corresponding homoallenic amine as judged by TLC (eluent 20% ethyl acetate in hexanes). The yellow solution was again filtered through a path of silica using ethyl acetate as eluent. The resulting solution was concentrated under reduced pressure to give a yellow oil. The residue was purified by flash chromatography using a gradient of ethyl acetate in hexanes (0 to 10%).



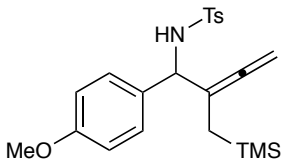
4-methyl-*N*-(1-phenyl-2-((trimethylsilyl)methyl)buta-2,3-dien-1-yl)benzenesulfonamide (2.63a): Obtained as a white solid (83 mg, 22 mmol, 73%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.60 (d, 2 H), 7.25-7.13 (m, 7 H), 5.06 (d, *J* = 7.99 Hz, 1 H), 4.95-4.88 (dq, *J* = 2.84, 9.77 Hz, 1 H), 4.84-4.77 (dq, *J* = 2.99, 9.77 Hz, 1 H), 4.64 (dt, *J* = 2.5, 7.67 Hz, 1H), 2.39 (s, 3 H), 1.07 (dt, *J* = 3.03, 15.05 Hz, 1 H), 0.99 (dt, *J* = 2.99, 15.05 Hz, 1 H), – 0.07 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.9, 142.99, 139.3, 137.7, 129.2, 128.4, 127.7, 127.6, 127.1, 102.7, 80.5, 59.3, 21.4, 18.3, -1.3; IR (thin film) 3276.5, 2953.6, 1955.4, 1329.6, 1161.7 cm^{-1}; HRMS (MALDI) calcd for $C_{21}H_{27}NO_2SSi$ (M + Na) 408.1429, found 408.1439.



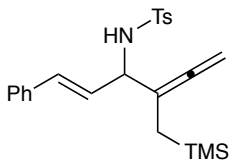
***N*-(1-(4-bromophenyl)-2-((trimethylsilyl)methyl)buta-2,3-dien-1-yl)-4-methylbenzenesulfonamide (2.63b):** Obtained as a clear oil (81 mg, 0.17 mmol, 58%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.55 (d, *J* = 8.42 Hz, 2 H), 7.31 (d, *J* = 8.42 Hz, 2 H), 7.17 (d, *J* = 8.01 Hz, 2 H), 7.06 (d, *J* = 8.43 Hz, 2 H), 5.14 (d, *J* = 8.09 Hz, 1 H), 4.9 (dq, *J* = 2.87, 10.03 Hz, 1 H), 4.8 (dq, *J* = 2.93, 10.09 Hz, 1 H), 4.59 (dt, *J* = 3.19, 7.36 Hz, 1H), 2.39 (s, 3 H), 1.15 (dt, *J* = 3.16, 15.01 Hz, 1 H), 0.9 (dt, *J* = 2.9, 15.1 Hz, 1 H), -0.7 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.7, 143.2, 138.3, 137.5, 131.4, 129.4, 129.3, 127.1, 121.7, 102.3, 80.9, 58.8, 21.4, 18.3, -1.2; IR (thin film) 3276.6, 1957.5, 1334.0, 1163.3 cm^{-1}; HRMS (MALDI) calcd for $C_{21}H_{26}NO_2SSi$ (M + Na) 486.0535, found 486.0552.



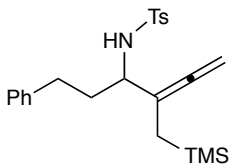
4-methyl-*N*-(1-(4-(trifluoromethyl)phenyl)-2-((trimethylsilyl) methyl)buta-2,3-dien-1-yl)benzenesulfonamide (2.63c): Obtained as a clear oil (27 mg, 0.06 mmol, 20%); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.50 (d, *J* = 8.28 Hz, 2 H), 7.48 (d, *J* = 7.87 Hz, 2 H), 7.21 (d, *J* = 8.14 Hz, 2 H), 7.11 (d, *J* = 8.14 Hz, 2 H), 5.16 (d, *J* = 7.17 Hz, 1 H), 4.93 (dq, *J* = 2.95, 10.15 Hz, 1 H), 4.87 (dq, *J* = 3.0, 10.15 Hz, 1 H), 4.67 (dt, *J* =3.02, 7.26 Hz, 1H), 2.34 (s, 3 H), 1.16 (dt, *J* = 2.93, 15.06 Hz, 1 H), 0.96 (dt, *J* = 2.70, 15.13 Hz, 1 H), -0.06 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.6, 143.2, 137.3, 129.2, 128.0, 127.0, 125.1 (q, *J* = 3.62) 102.2, 81.0, 58.9, 21.3, 18.3, -1.3; IR (thin film) 2955.94, 1955.69, 1325.9, 1162.1 cm^{-1}; HRMS (MALDI) calcd for $C_{22}H_{26}F_3NO_2SSi$ (M + Na) 476.1303, found 476.1292.



***N*-(1-(4-methoxyphenyl)-2-((trimethylsilyl)methyl)buta-2,3-dien-1-yl)-4-methyl benzenesulfonamide (2.63d):** Obtained as a clear oil (66 mg, 0.16 mmol, 53%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.59 (d, *J* = 8.45 Hz, 2 H), 7.18 (d, *J* = 7.74 Hz, 2 H), 7.06 (d, *J* = 9.45 Hz, 2 H), 6.47 (d, *J* = 8.80 Hz, 2 H), 5.09 (d, *J* = 7.60 Hz, 1 H), 4.9 (dq, *J* = 3.0, 9.71 Hz, 1 H), 4.7 (dq, *J* = 3.0, 9.78 Hz, 1 H), 4.59 (dt, *J* = 3.18, 7.54 Hz, 1H), 3.77 (s, 3H), 2.38 (s, 3 H), 1.16 (dt, *J* = 2.95, 15.21 Hz, 1 H), 0.89 (dt, *J* = 2.71, 15.2 Hz, 1 H), -0.06 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.8, 159.1, 142.8, 137.8, 131.4, 129.2, 128.8, 127.2, 113.7, 102.7, 80.4, 58.8, 55.2, 21.4, 18.4, -1.2; IR (thin film) 3277.4, 3032.9, 2897.9, 1955.6, 1327.6, 1160.6 cm^{-1}; HRMS (MALDI) calcd for $C_{22}H_{29}NO_2SSi$ (M + Na) 438.1535, found 438.1555.

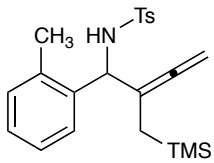


4-methyl-*N*-(1-phenyl-4-((trimethylsilyl)methyl)hexa-1,4,5-trien-3-yl)benzenesulfon-amide (2.53e): Obtained as a clear oil (20 mg, 0.05 mmol, 16%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.71 (d, *J* = 8.45 Hz, 2 H), 7.30-7.14 (m, 7 H), 6.33 (d, *J* = 15.74 Hz, 1 H), 5.76 (dd, *J* = 7.75, 15.56 Hz, 1 H), 4.83 (m, 2 H), 4.77 (d, *J* = 8.07 Hz, 1 H), 4.21 (m, 1H), 2.34 (s, 3 H), 1.29 (dt, *J* = 1.29, 15.0 Hz, 1 H), 1.16 (dt, *J* = 2.71, 15.12 Hz, 1 H), -0.02 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.07, 143.2, 136.1, 132.2, 129.4, 128.4, 127.8, 127.3, 127.2, 126.4, 101.1, 80.1, 58.0, 21.3, 18.07, -1.2; IR (thin film) 3271.9, 2953.05, 1953.8, 1328.9, 1160.6 cm^{-1} ; HRMS (-ESI) calcd for $C_{23}H_{29}NO_2SSi$ (M - H) 440.1610, found 410.1623.

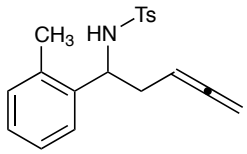


4-methyl-*N*-(1-phenyl-4-((trimethylsilyl)methyl)hexa-4,5-dien-3-yl)benzene-sulfonamide (2.63f): Obtained as a clear oil (103 mg, 0.25 mmol, 84%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.74 (d, *J* = 8.26 Hz, 2 H),

7.32-7.08 (m, 7 H), 4.82-4.63 (m, 3 H), 3.6 (m, 1H), 2.63 (dt, *J* = 5.84, 9.64 Hz, 2 H), 2.42 (s, 3 H), 1.96 (m, 1 H), 1.73 (m, 1H), 1.14 (dt, *J* = 3.13, 15.27 Hz, 1 H), 0.9 (dt, *J* = 2.97, 15.22 Hz, 1 H), -0.1 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.4, 143.2, 141.4, 137.9, 129.4, 128.4, 128.3, 127.3, 125.8, 101.7, 79.3, 55.9, 36.1, 31.6, 21.4, 17.6, -1.3; IR (thin film) 3278.3, 1955.9, 1332.7, 1162.5 cm^{-1}; HRMS (MALDI) calcd for $C_{23}H_{31}NO_2SSi$ (M + Na) 436.1743, found 436.1750.

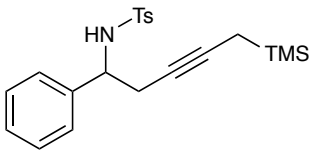


4-methyl-*N*-(1-(*o*-tolyl)-2-((trimethylsilyl)methyl)buta-2,3-dien-1-yl)benzenesulfon-amide (2.63g): Obtained as a white solid (35 mg, 0.09 mmol, 30%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.59 (d, *J* = 8.43 Hz, 2 H), 7.16 (*J* = 8.28 Hz, 2 H), 7.13-7.03 (m, 4 H), 4.96 (s, 2 H), 4.86 (m, 1H) 4.62 (m, 1 H), 2.38 (s, 3 H), 2.33 (s, 3H), 1.16 (dt, *J* = 3.02, 15.13 Hz, 1 H), 0.89 (dt, *J* = 2.77, 15.16 Hz, 1 H), -0.05 (s, 0 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.3, 142.8, 137.9, 137.1, 136.4, 130.6, 129.1, 127.6, 127.3, 127.1, 126.0, 102.5, 80.3, 56.1, 21.4, 19.1, 18.2, -1.3; IR (thin film) 3279.5, 1955.4, 1599.1, 1330.9, 1161.2.8 cm^{-1}; HRMS (+ESI) calcd for $C_{19}H_{21}NO_2S$ (M + Na) 422.1586, found 422.1598.

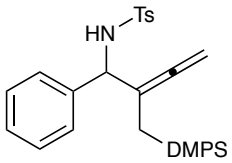


4-methyl-*N*-(1-(*o*-tolyl)penta-3,4-dien-1-yl)benzenesulfonamide (2.69g): Obtained as a white solid (34 mg, 0.10 mmol, 35%) ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.53 (d, *J* = 8.28 Hz, 2H), 7.12 (d, *J* = 7.95 Hz, 2 H), 7.09-6.98 (m, 4 H), 4.87 (d, *J* = 6.30 Hz, 1 H), 4.85 (quint, *J* = 7.02 Hz, 1H), 4.65 (m, 3 H), 2.38 (m, 2H), 2.36 (s, 3H), 2.21 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.7, 143.1, 138.2, 137.4, 134.8, 130.3, 129.2, 127.2, 127.0, 126.1, 124.9, 85.1, 75.3, 53.5, 36.0, 21.4, 19.1; IR (thin

film) 3276.1, 1955.5, 1330.8, 1157.8 cm^{-1}; HRMS (+ESI) calcd for $C_{19}H_{21}NO_2S$ (M + H) 328.1371, found 328.1360.

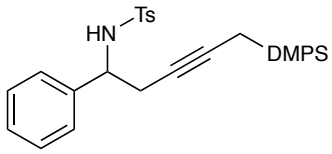


4-methyl-*N*-(1-phenyl-5-(trimethylsilyl)pent-3-yn-1-yl)benzenesulfon-amide (2.64): Obtained as a white solid. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.61 (d, *J* = 8.3 Hz, 2 H), 7.22-7.14 (m, 7 H), 5.15 (d, *J* = 7.11 Hz, 1 H), 4.42 (q, *J* = 6.05 Hz, 1 H), 2.58 (dt, *J* = 2.69, 5.89 Hz, 2 H), 2.39 (s, 3 H), 1.38 (t, *J* = 2.69 Hz, 2 H), – 0.03 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1, 139.7, 137.3, 129.3, 128.3, 128.2, 127.6, 127.5, 127.1, 126.6, 82.1, 72.8, 56.0, 27.6, 21.4, 6.9, -2.1; IR (thin film) 3257.4, 3031.8, 2223.0, 1330.0, 1161.1 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{27}NO_2SSi$ (M + Na) 408.1429, found 408.1204.

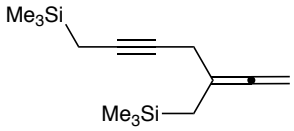


***N*-(2-((dimethyl(phenyl)silyl)methyl)-1-phenylbuta-2,3-dien-1-yl)-4-methylbenzenesulfonamide (2.66):** Following the procedure described for the general synthesis of (silylmethyl)allenic amines. After the reaction mixture was stirred for 48 h as described in the general procedure, 2 M HCl (1 mL) and ethyl acetate (1 -2 mL) were added to the gray suspension and the green mixture was stirred for 1 h. The resulting mixture was extracted with 3 portions of ethyl acetate. Combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography using a gradient of ethyl acetate in hexanes (0 to 10%) to give the desired product as a white solid (69 mg, 0.15 mmol, 52%). ^1H NMR ($CDCl_3$, 300 MHz) δ 7.52 (d, *J* = 8.39 Hz, 2 H), 7.42-7.31 (m, 5H), 7.20-7.12 (m, 5 H), 7.01 (m, 2 H), 4.99 (d, *J* = 7.6 Hz, 1 H), 4.83 (dq, *J* = 2.6, 9.86 Hz, 1 H), 4.7 (dq, *J* = 2.96, 9.97 Hz, 1 H), 4.57 (dt, *J* =3.20, 7.66 Hz, 1H), 2.38 (s, 3 H), 1.43 (dt, *J* = 2.71, 15.2 Hz, 1 H), 1.17 (dt, *J* = 2.82,

15.1 Hz, 1 H), 0.23 (s, 3 H), 0.19 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.03, 142.8, 139.1, 138.2, 137.6, 133.5, 129.17, 129.11, 128.3, 127.7, 127.6, 127.5, 127.1, 102.2, 80.5, 59.1, 21.4, 17.5, -2.7, -3.0; IR (thin film) 3774.3, 2954.6, 1955.4, 1329.2, 1161.3 cm^{-1}; HRMS (MALDI) calcd for $C_{26}H_{29}NO_2SSi$ (M + Na) 470.1586, found 470.1601.



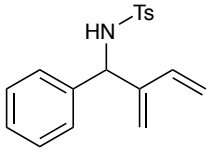
***N*-(5-(dimethyl(phenyl)silyl)-1-phenylpent-3-yn-1-yl)-4-methyl-benzenesulfonamide (2.67):** Inside a Nitrogen atmosphene Drybox, a mixture of $CrCl_2$ (3.6 mg, 0.03 mmol) and Mn powder 325-mesh (33mg, 0.66 mmol) were added to a 2-dram vial. The vial was capped with a Teflon lid and it was removed from the drybox. The tosylimine (0.3 mmol) was added to the mixture and the vial was flushed with argon. Dry THF (2 mL) was added via syringe and a brown suspension was formed. This was followed of (4-bromobut-2-yn-1-yl)dimethyl(phenyl)silane (120 mg, 0.45 mmol). The mixture was stirred at room temperature for 48 h. 2 M HCl (1 mL) and ethyl acetate (1 -2 mL) were added to the gray suspension and the green mixture was stirred for 1 h. The resulting mixture was extracted with 3 portions of ethyl acetate. Combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure to give a tan oil. The residue was purified by flash chromatography using a gradient of ethyl acetate in hexanes (0 to 10%) to give the desired product as a yellow oil (56 mg, 0.12 mmol, 42%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.58 (d, *J* = 8.15 Hz, 2 H), 7.49 (m, 2 H), 7.39 (m, 3 H), 7.20-7.15 (m, 5 H), 7.09-7.05 (m, 2 H), 5.05 (d, *J* = 7.1 Hz, 1 H), 4.42 (q, *J* = 5.65, 11.83 Hz, 1 H), 2.57 (dt, *J* = 2.6, 2.6, 5.6 Hz, 2 H), 2.39 (s, 3 H), 1.63 (t, *J* = 2.5 Hz, 2 H), 0.29 (s, 3H), 0.27 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.6, 143.1, 140.9, 136.9, 133.0, 132.9, 132.8, 131.7, 131.4, 130.9, 130.5, 130.1; IR (thin film) 3276.6, 3067.6, 2223.2, 1330.6, 1161.1 cm^{-1}; HRMS (MALDI) calcd for $C_{26}H_{29}NO_2SSi$ (M + Na)) 470.1586, found 470.3550.



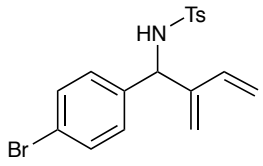
(5-vinylidenehex-2-yne-1,6-diyl)bis(trimethylsilane) (2.5b): Obtained as a clear oil ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.69 (q, *J* = 2.82 Hz, 2 H), 2.87 (q, *J* = 2.93 Hz, 2 H), 1.46 (t, *J* = 2.72 Hz, 2 H), 1.42 (t, *J* = 2.56 Hz, 2 H), 0.10 (s, 9 H), 0.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.4, 101.8, 97.8, 79.2, 75.5, 25.6, 20.1, 7.0, -1.1, -2.0; IR (thin film) 2955.5, 2895.8, 2220.5, 1957.9, 1416.6 cm^{-1}; HRMS (MALDI) calcd for $C_{14}H_{26}Si2$ (M - H) 449.1489, found 249.1482.

2.5.17 General Method for the preparation of 2-aminomethyl-1,3-dienes

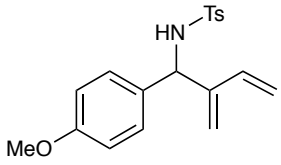
Allene (0.21mmol) was dissolved in THF (2 mL). TBAF (1M in THF, 0.21 mL, 0.21 mmol) was added and the solution. After 3h an extra equivalent of TBAF (1M in THF, 0.21 mL, 0.21 mmol) was added and the mixture was stirred for 21 hours at r.t. The yellow solution was filtered though a path of silica using ethyl acetate as eluent. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography using a gradient of ethyl acetate in hexanes (0 to 12%) to afford the desired diene.



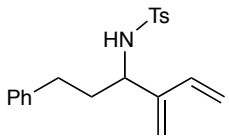
4-methyl-*N*-(2-methylene-1-phenylbut-3-en-1-yl)benzenesulfonamide (2.70a): Obtained as a white solid (53 mg, 0.17 mmol, 81%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.68 (d, *J* = 8.43 Hz, 2 H), 7.23 (m, 5 H) 7.16 (m, 2 H), 6.18 (dd, *J* = 11.42, 17.72 Hz, 1 H), 5.26-5.22 (m, 3 H), 5.13 (d, *J* = 0.78 Hz, 1 H), 5.08 (d, *J* = 17.96 Hz, 1 H), 5.02 (d, *J* = 11.46 Hz, 1 H), 4.84 (d, *J* = 7.91 Hz, 1H) 2.4 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.4, 143.2, 139.0, 137.4, 135.5, 129.4, 128.5, 127.7, 127.2, 127.1, 118.2, 116.0, 58.6, 21.5; IR (thin film) 3283.1, 1636.9, 1598.7, 1326.1, 1159.8 cm^{-1}; ; HRMS (ESI) calcd for $C_{18}H_{19}NO_2S$ (M + Na) 336.1034, found 336.1028.



***N*-(1-(4-bromophenyl)-2-methylenebut-3-en-1-yl)-4-methylbenzene-sulfonamide (2.70b):** Obtained as a white solid (49 mg, 0.13 mmol, 65%, 74% conversion). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.61 (d, *J* = 8.30 Hz, 2 H), 7.33 (d, *J* = 8.56 Hz, 2 H), 7.21 (d, *J* = 8.56 Hz, 2 H), 7.02 (d, *J* = 8.56 Hz, 2 H), 6.18 (dd, *J* = 11.27, 17.66 Hz, 1 H), 5.24-4.99 (m, 6 H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.1, 143.5, 138.0, 135.2, 131.5, 129.4, 128.9, 127.2, 121.6, 118.6, 116.3, 58.0, 21.5; IR (thin film) 3277.0, 1597.1, 1327.8, 1184.3 cm^{-1}; HRMS (-ESI) calcd for $C_{18}H_{18}BrNO_2S$ (M - H) 390.0163, found 390.0175.

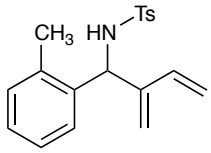


***N*-(1-(4-methoxyphenyl)-2-methylenebut-3-en-1-yl)-4-methyl benzene-sulfonamide (2.70d):** Obtained as a white solid (53 mg, 0.16 mmol, 84%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.64 (d, *J* = 8.53 Hz, 2 H), 7.21 (d, *J* = 8.14 Hz, 2 H), 7.02 (d, *J* = 9.31 Hz, 2 H), 6.72 (d, *J* = 8.53 Hz, 2 H), 6.19 (dd, *J* = 11.33, 18.03 Hz, 1 H), 5.22 (s, 1 H), 5.17 (d, *J* = 7.69 Hz, 1 H), 5.15 (s, 1 H), 5.05 (d, *J* = 17.94 Hz, 1H), 5.00 (d, *J* = 11.35 Hz, 1 H) 4.88 (d, *J* = 6.96 Hz, 1 H), 3.79 (s, 3 H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.1, 144.5, 143.2, 137.5, 135.6, 131.1, 129.3, 128.4, 127.2, 117.8, 115.8, 113.9, 58.0, 55.2, 21.5; IR (thin film) 3434.6, 1610.8, 1510.6, 1323.0, 1158.2 cm^{-1}; HRMS (-ESI) calcd for $C_{19}H_{21}NO_3S$ (M + Li) 350.1402, found 350.1408.



4-methyl-*N*-(4-methylene-1-phenylhex-5-en-3-yl)benzenesulfonamide (2.70f): Obtained as a white solid (78 mg, 0.23 mmol, 92%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.73 (d, *J* = 8.30 Hz, 2 H), 7.31-7.20 (m, 5H), 7.11 (d, *J* = 6.84 Hz, 2 H), 6.15 (dd, *J* = 10.93, 17.77 Hz, 1 H), 5.17 (d, *J* = 8.10 Hz, 1 H), 5.05 (d, *J* =

17.96 Hz, 1H), 5.03 (s, 1 H), 5.0 (d, *J* = 11.99 Hz, 1 H), 4.89 (s, 1H), 4.09 (q, *J* = 7.24 Hz, 1H), 2.62 (m, 2 H), 2.44 (s, 3 H), 1.92 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.4, 142.2, 141.0, 137.7, 135.5, 129.4, 128.5, 128.4, 127.2, 126.0, 115.7, 114.8, 54.4, 37.1, 31.9, 21.5; IR (thin film) 3276.2, 2864.0, 1597.1, 1318.1, 1162.2 cm^{-1}; HRMS (+ESI) calcd for $C_{20}H_2NO_2S$ (M + H) 342.1528, found 342.1537.

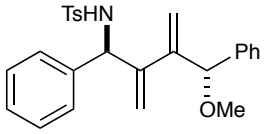


4-methyl-*N*-(2-methylene-1-(*o*-tolyl)but-3-en-1-yl)benzenesulfonamide (2.70g): Obtained as a white solid (24 mg, 0.073 mmol, 73%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.59 (d, *J* = 8.47 Hz, 2 H), 7.16 (d, *J* = 8.28 Hz, 2 H), 7.11-6.94 (m, 4 H), 6.26 (dd, *J* = 11.18, 17.89 Hz, 1 H), 5.52 (d, *J* = 6.96 Hz, 1 H), 5.19 (d, *J* = 17.57 Hz, 1 H), 5.19 (s, 1 H), 5.04 (d, *J* = 11.10 Hz, 1H), 4.88 (s, 1 H), 4.74 (d, *J* = 7.12 Hz, 1 H), 2.37 (s, 3 H), 2.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.4, 143.1, 137.7, 136.7, 135.9, 135.7, 130.6, 129.6, 127.6, 127.1, 126.6, 125.9, 118.6, 115.3, 54.6, 21.4, 18.9; IR (thin film) 3271.0, 3064.0, 1595.5, 1318.8, 1185.6 cm^{-1}; HRMS (+ESI) calcd for $C_{19}H_{21}NO_3S$ (M + H) 328.1371, found 328.1379.

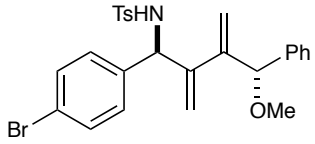
2.5.18 General Method for the preparation of functionalized 1,3-dienes

The allene (0.15 mmol) was dissolved in CH_2Cl_2 (1 mL) and cooled to –78°C. Then, a solution of dimethylacetal benzaldehyde (0.16 mmol) and $BF_3{\cdot}Et_2O$ (0.16 mmol) in CH_2Cl_2 (1 mL) was added to the allene solution dropwise followed by one extra mL of CH_2Cl_2. The mixture was stirred at –78°C for one hour. After this time, one more portion of dimethylacetal benzaldehyde (0.8 mmol) and $BF_3{\cdot}Et_2O$ (0.8 mmol) were added to the reaction mixture. More acid and acetal (1 equiv) may be added to accelerate the reaction. Reaction was monitored by TLC and after completion, a saturated solution of $NaHCO_3$ (1 mL) and ethyl acetate (1 mL) were

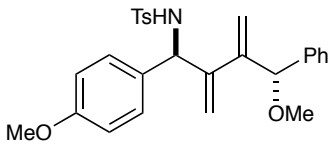
added to the red solution. The mixture was extracted with three portions of ethyl acetate. The combined organic phased were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography (0 to 12 % ethyl acetate in hexanes) to give the desired diene.



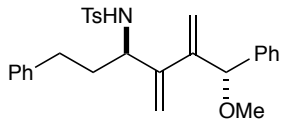
***N*-(3-(methoxy(phenyl)methyl)-2-methylene-1-phenylbut-3-en-1-yl)-4-methylbenzenesulfonamide (2.73a):** Obtained as a clear oil (60 mg, 0.13 mmol, 92%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.53 (d, *J* = 7.53 Hz, 2H), 2.33- 7.12 (m, 10 H), 7.01 (m, 2H), 5.19-4.85 (m, 6H), 4.70 (s, 1 H), 3.24 (d, *J* = 0.56 Hz, 3 H), 2.38 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145. 4, 145.0, 143.0, 139.0, 139.1, 137.4, 129.3, 128.3, 127.8, 127.5, 127.4, 127.3, 117.4, 116.5, 85.0, 60.4, 56.9, 21.5; IR (thin film) 3278.0, 3062.0, 1598.7, 1327.5, 1185.7 cm^{-1}; HRMS (+ESI) calcd for $C_{26}H_{27}NO_3S$ (M + Li) 440.1872, found 440.1861.



***N*-(1-(4-bromophenyl)-3-(methoxy(phenyl)methyl)-2-methylene but-3-en-1-yl)-4-methylbenzenesulfonamide (2.73b):** Obtained as a clear oil (43 mg, 0.084 mmol, 93%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.5 (d, *J* = 8.21 Hz, 2 H), 7.33-7.12 (m, 10 H), 6.88 (d, *J* = 8.41 Hz, 2 H), 5.17-5.91 (m, 5 H), 4.81 (s, 1 H), 4.70 (s, 1H), 3.26 (s, 3H), 2.40 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.3, 144.8, 143.33, 139.1, 138.1, 137.2, 131.3, 129.3, 129.2, 129.0, 128.3, 127.9, 127.2, 127.1, 117.8, 116.9, 85.2, 60.0, 56.9, 21.5; IR (thin film) 3278.3, 3088.8, 1599.5, 1332.3, 1187.4 cm^{-1}; HRMS (+ESI) calcd for $C_{26}H_{26}BrNO_3S$ (M + Li) 518.0977 found 518.0971.



***N*-(3-(methoxy(phenyl)methyl)-1-(4-methoxyphenyl)-2-methylenebut-3-en-1-yl)-4-methylbenzenesulfonamide (2.73c):** Obtained as a clear oil (49 mg, 0.10 mmol, 95%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.56 (d, *J* = 8.21 Hz, 2 H), 7.39-7.15 (m, 8 H), 6.95 (d, *J* = 8.7 Hz, 2H), 6.72 (d, *J* = 8.7 Hz, 2 H), 5.20-4.93 (m, 6 H), 4.73 (s, 1H), 3.78 (s, 3H), 3.28 (s, 3H), 2.42 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 145.4, 145.4, 145.1, 143.0, 139.5, 139.5, 137.5, 131.2, 129.3, 128.3, 127.8, 127.3, 127.2, 116.5, 113.7, 85.1, 59.8, 56.9, 55.2, 21.5; IR (thin film) 3279.6, 3062.0, 1599.4, 1325.4, 1159.7 cm^{-1}; HRMS (+ESI) calcd for $C_{27}H_{29}NO_4S$ (M + Li) 470.1977 found 470.1971.



N-(5-(methoxy(phenyl)methyl)-4-methylene-1-phenylhex-5-en-3-yl)-4-methylbenzenesulfonamide: Obtained as a clear oil (79 mg, 0.17 mmol, 78%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.62 (d, *J* = 8.32 Hz, 2 H), 7.35-7.18 (m, 10 H), 7.07 (d, *J* = 8.9 Hz, 2H), 5.30 (d, *J* = 7.85 Hz, 1H), 5.16 (s, 1H), 5.04 (s, 1H), 4.9 (s, 1H), 4.83 (s, 1H), 4.7 (s, 1H), 4.0 (q, *J* = 7.15 Hz, 1H), 3.3 (s, 3H), 2.51 (m, 2H), 2.43 (s, 3H), 1.77 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.7, 146.1, 143.0, 141.2, 139.2, 137.8, 129.4, 128.5, 128.3, 128.2, 127.8, 127.3, 127.2, 125.9, 115.7, 115.3, 84.7, 56.9, 56.2, 36.7, 31.8, 21.5; IR (thin film) 3282.7, 3085.7, 1599.5, 1323.5, 1158.4 cm^{-1}; HRMS (+ESI) calcd for $C_{28}H_{31}NO_3S$ (M + Li) 468.2185 found 468.2177.

3. SUMMARY AND CONCLUSIONS

In summary, we have developed a highly regioselective, efficient method for the synthesis of (trimethylsilyl)methylallenic alcohols and shown their further transformation into 1,3-butadien-2-ylcarbinols. Allenic alcohols were obtained from the chromium-catalyzed nucleophilic addition of (4-bromobut-2-yn-1-yl)trimethylsilane to aldehydes in a Nozaky-Hiyama-Kishi type reaction. The use of (4-bromobut-2-yn-1-yl)trimethylsilane as a diene equivalent, strongly favors the formation of homoallenyl alcohols over their propargylic isomers. Several analogues of the bis(oxazoline) carbazole compounds were synthesized the coupling of di-halocarbazoles and a variety of boronic acids, followed by halogenation, carbonylative amidation and cyclization. Bis(oxazoline) carbazoles are good ligands for this chromium-catalyzed addition reaction, affording chiral alcohols in generally good yields and enantioselectivities. Versatile allenic alcohol adducts can be succesfully converted to 1,3-butadien-2-ylcarbinols by desilylation using TBAF or iodinated for further functionalization.
In addition, we have developed a method for the synthesis of 3° 1,3-butadien-2-ylcarbinols from the chromium-catalyzed addition of (4-bromobut-2-ynyl)trimethylsilane to ketones. This is, to the best of our knowledge, the first chromium-catalyzed nucleophilic addition to ketones to afford 3° allenylalcohols.

Finally, the scope of this method was expanded of the synthesis 2-aminomethyl-1,3-dienes from tosyl-imines. The presence of an electron withdrawing tosyl group is fundamental to increase the reactivity of the imines towards nucleophilic additions. Interestingly, the regioselectivity of the allenylation reaction was drastically affected by the presence of a bulky tosyl group in the substrate leading to the formation of regioisomeric mixtures not observed previously. The nature of the substituent in the imine affects the isomer ratio, with smaller substituents favoring the formation of the desired allenic amine. Allenic imines were desilylated

for the synthesis of 2-aminomethyl-1,3-dienes and furthermore, other electrophiles such as (dimethoxymethyl)benzene can be used in the preparation of more complex 1,2-dienes.

The development of this methodology provided a novel route for the preparation of a variety of highly functionalized 1,3-dienes. Thus, making this transformation a valuable tool for the synthesis of more complex organic compounds.

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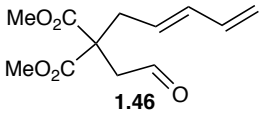
APPENDIX A

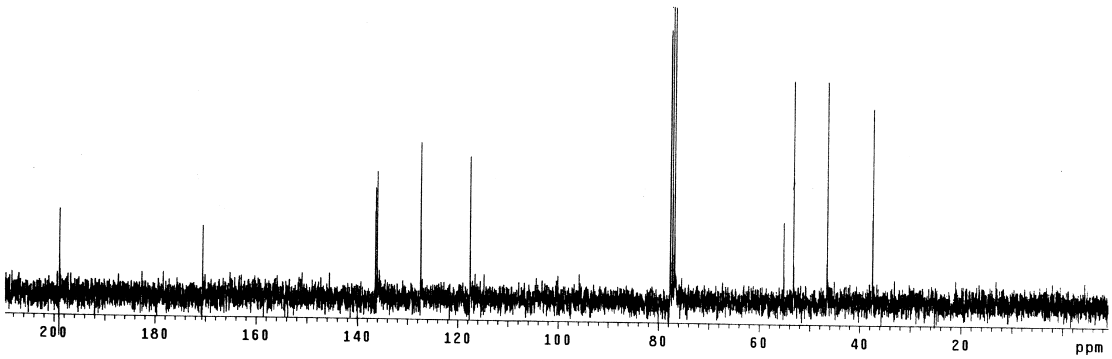
^{1}H AND ^{13}C NMR SPECTRA

^{1}H NMR ($CDCl_3$, 300 MHz)



1.46

^{13}C NMR ($CDCl_3$, 75 MHz)



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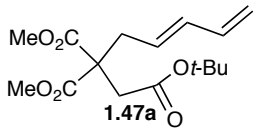

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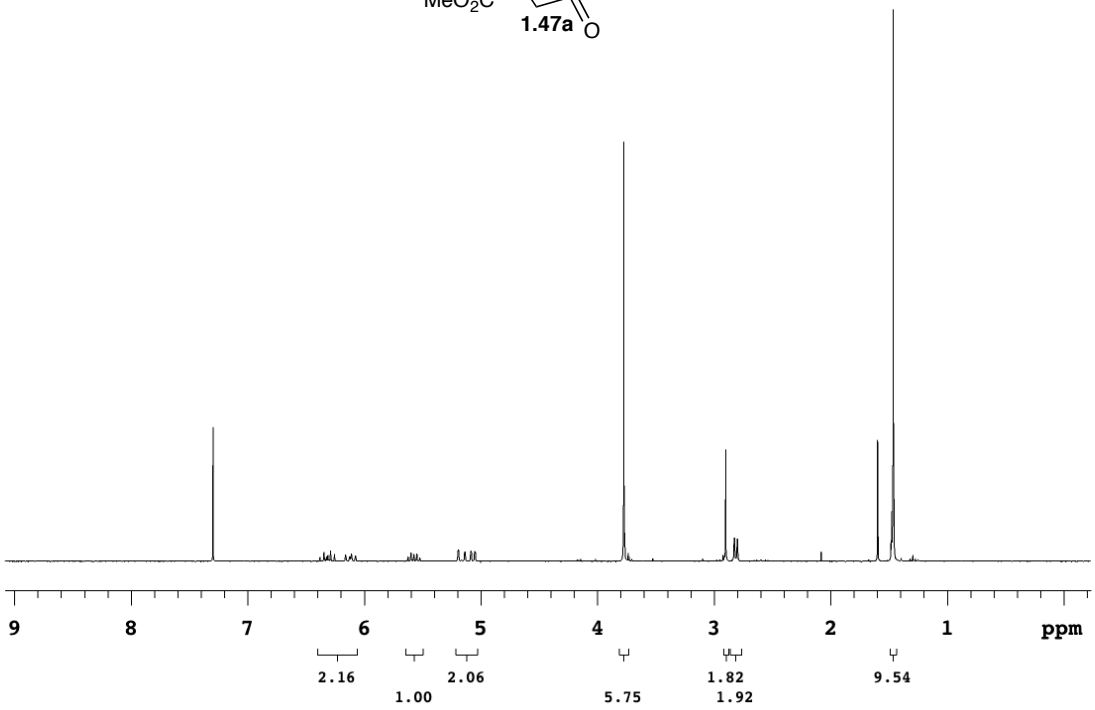

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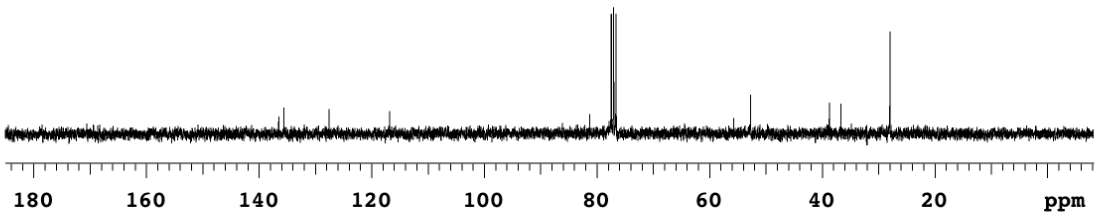

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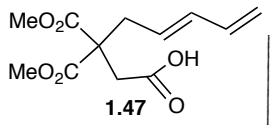

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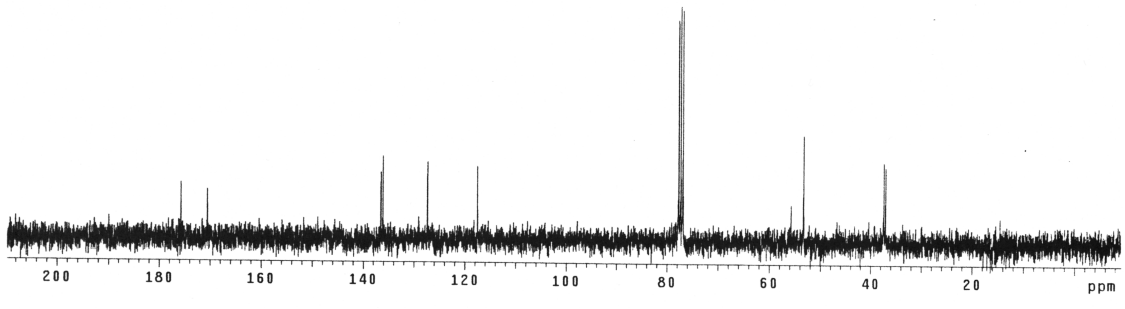

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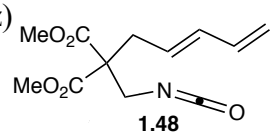

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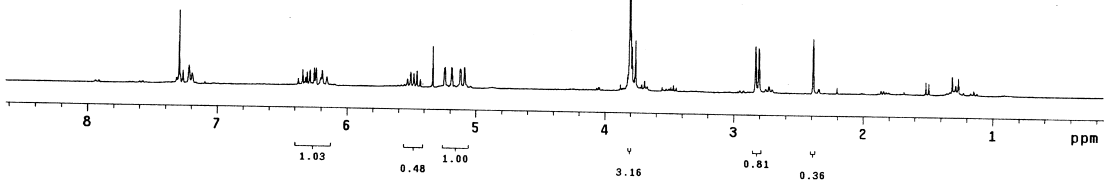

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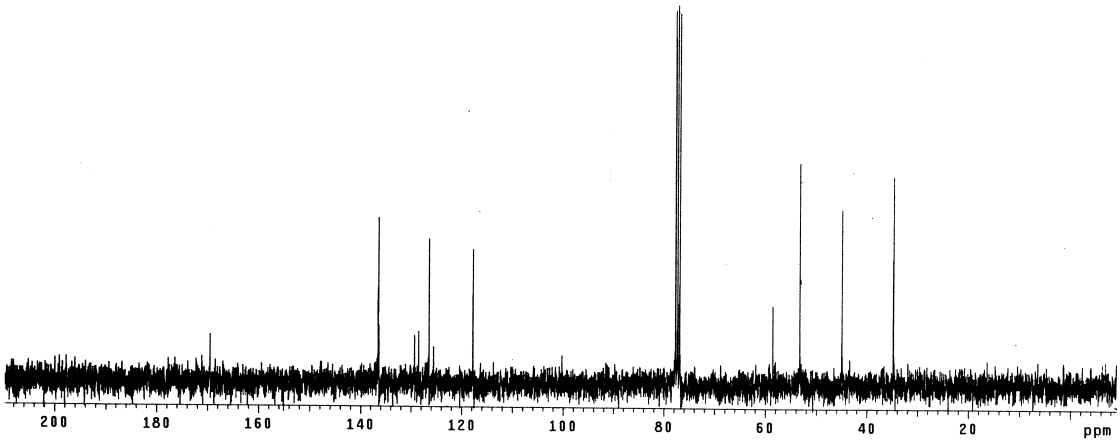

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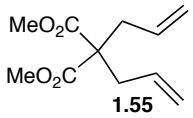

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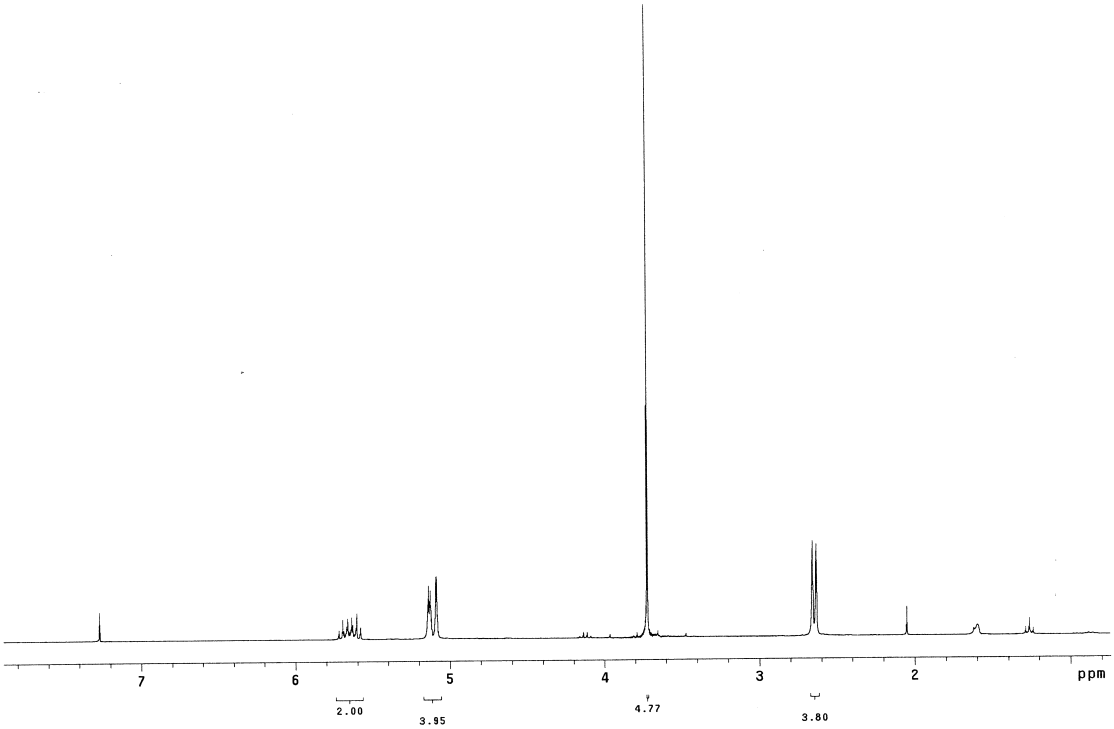

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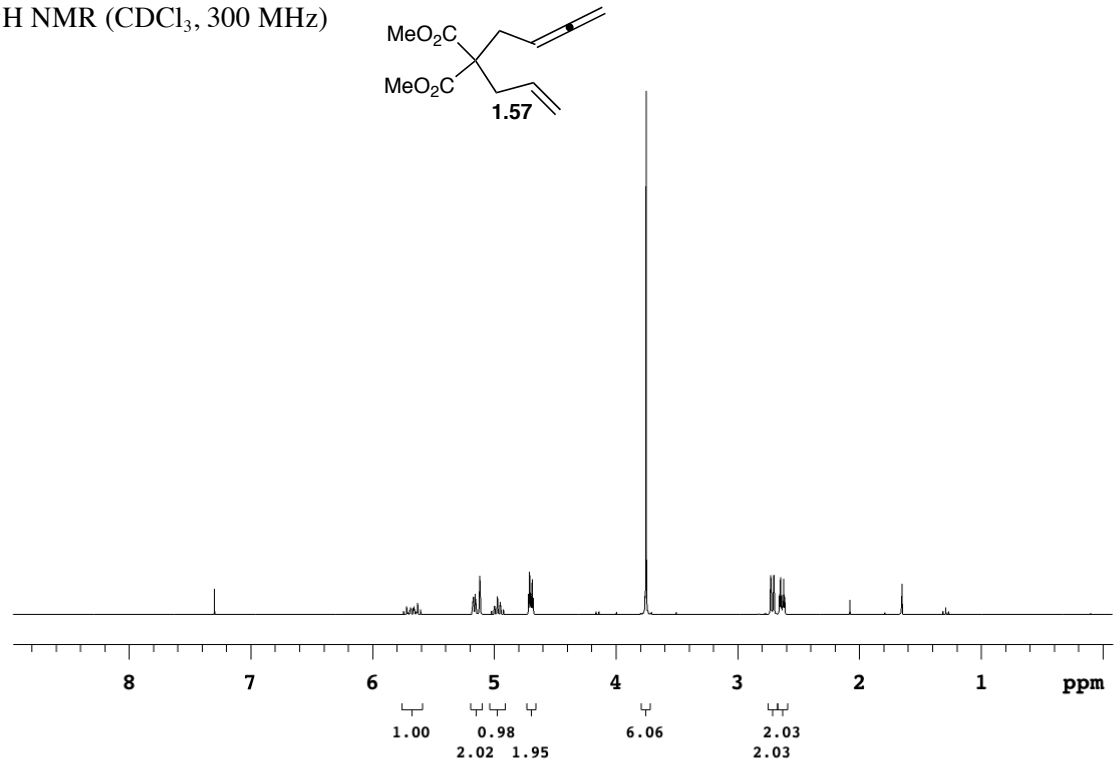

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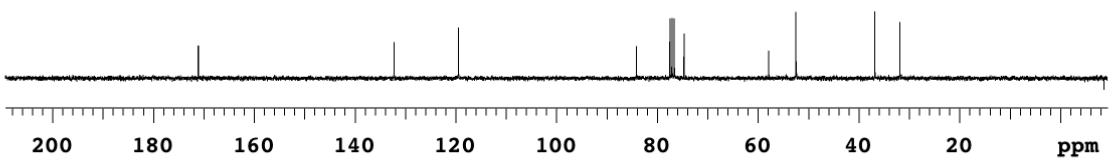

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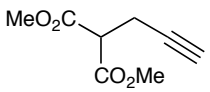

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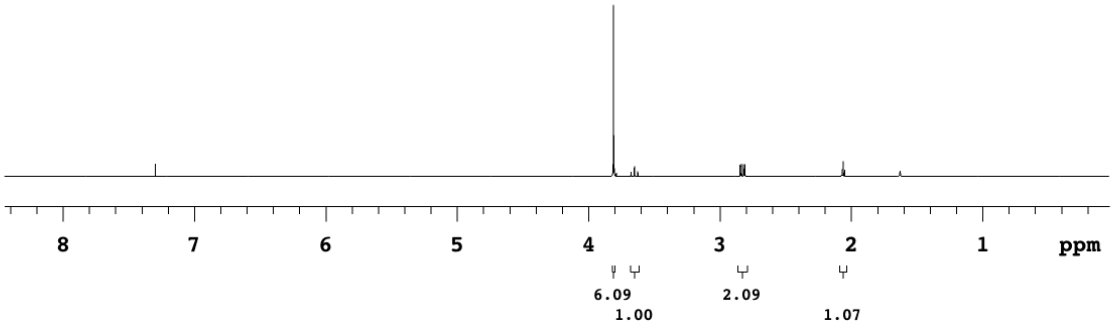

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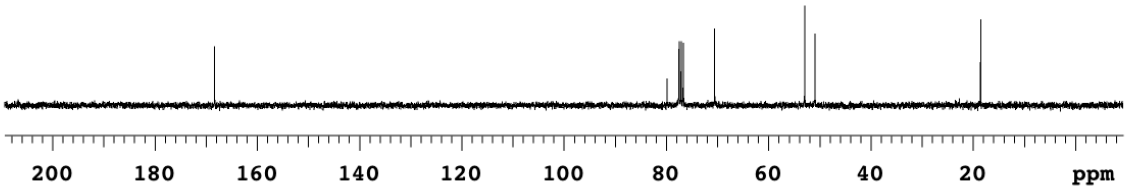

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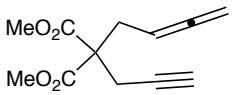

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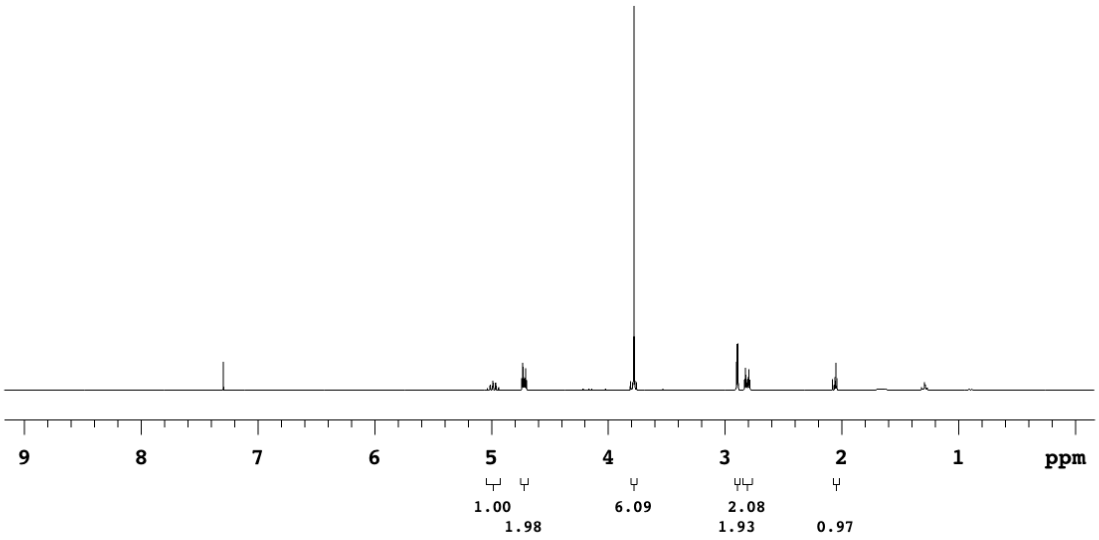

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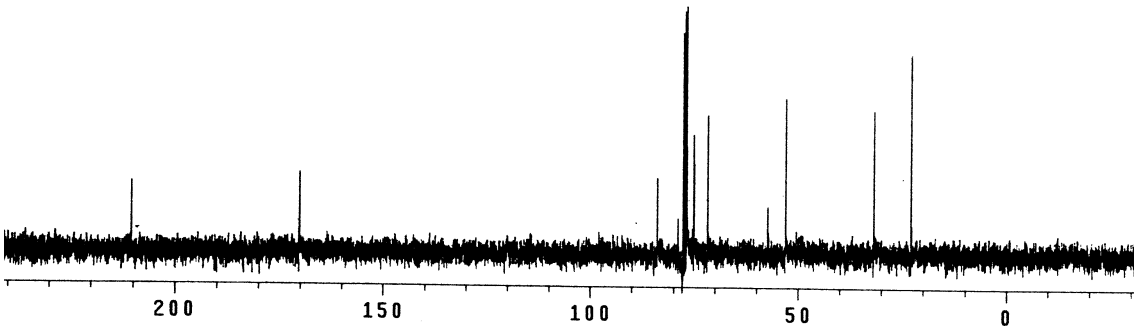

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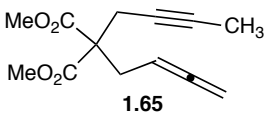

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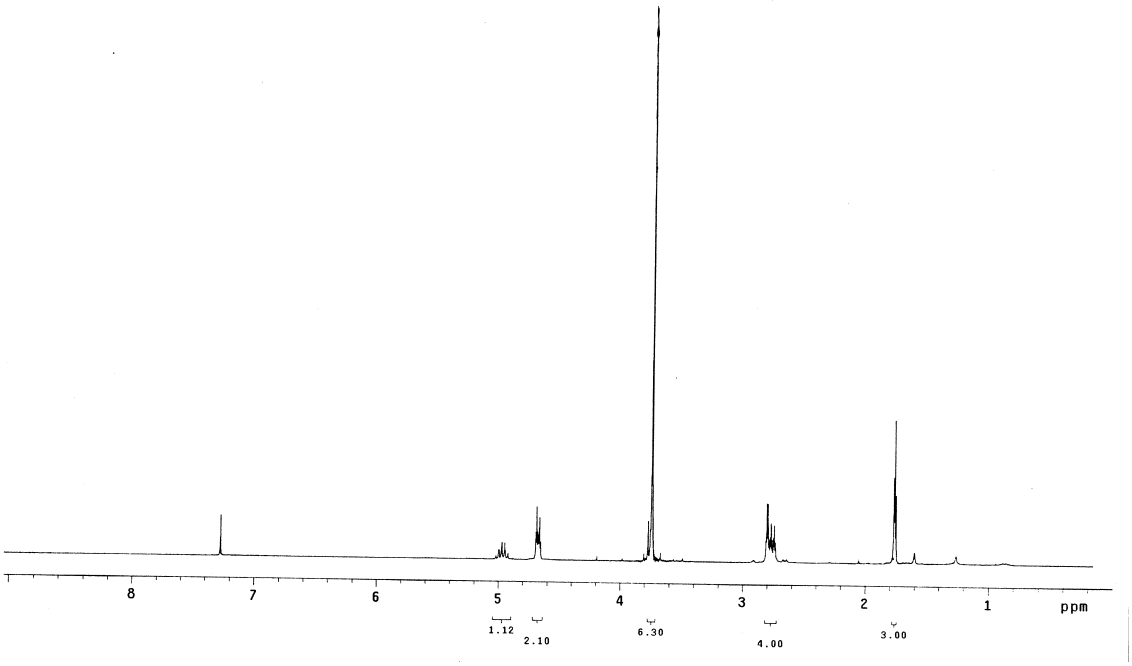

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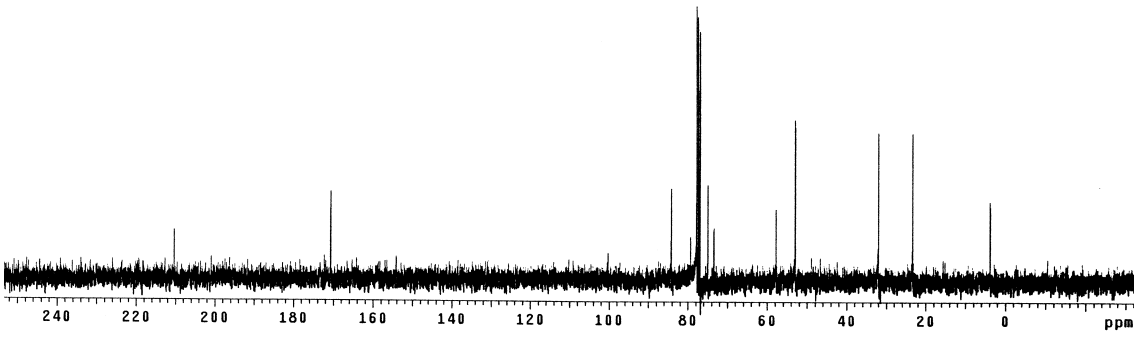

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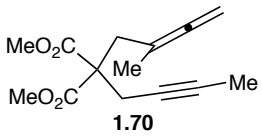

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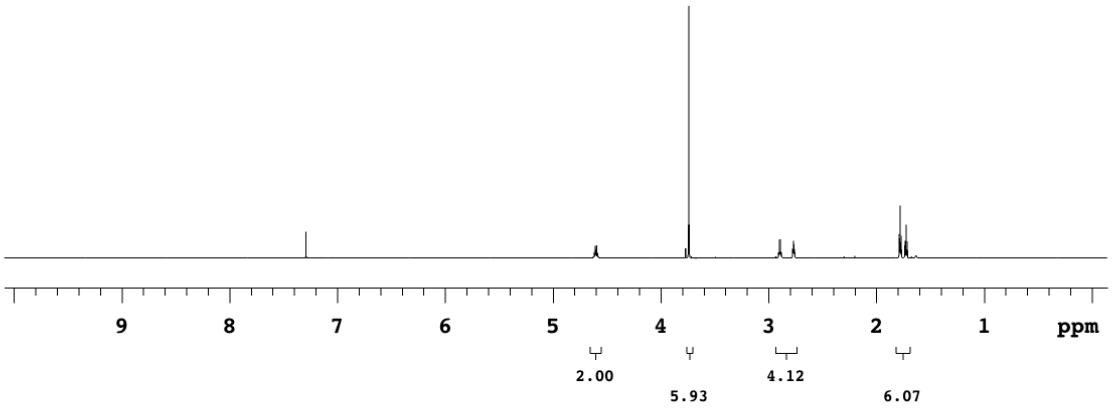

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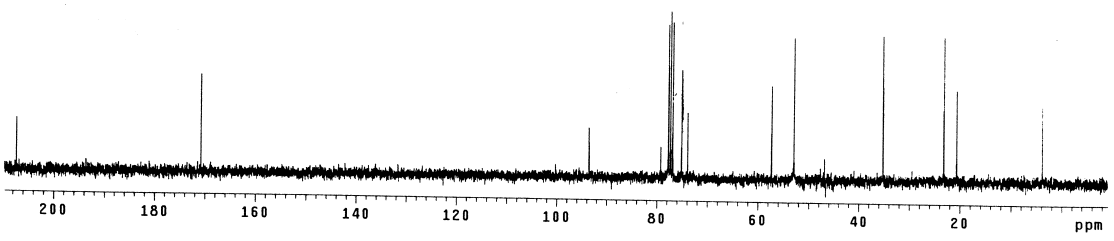

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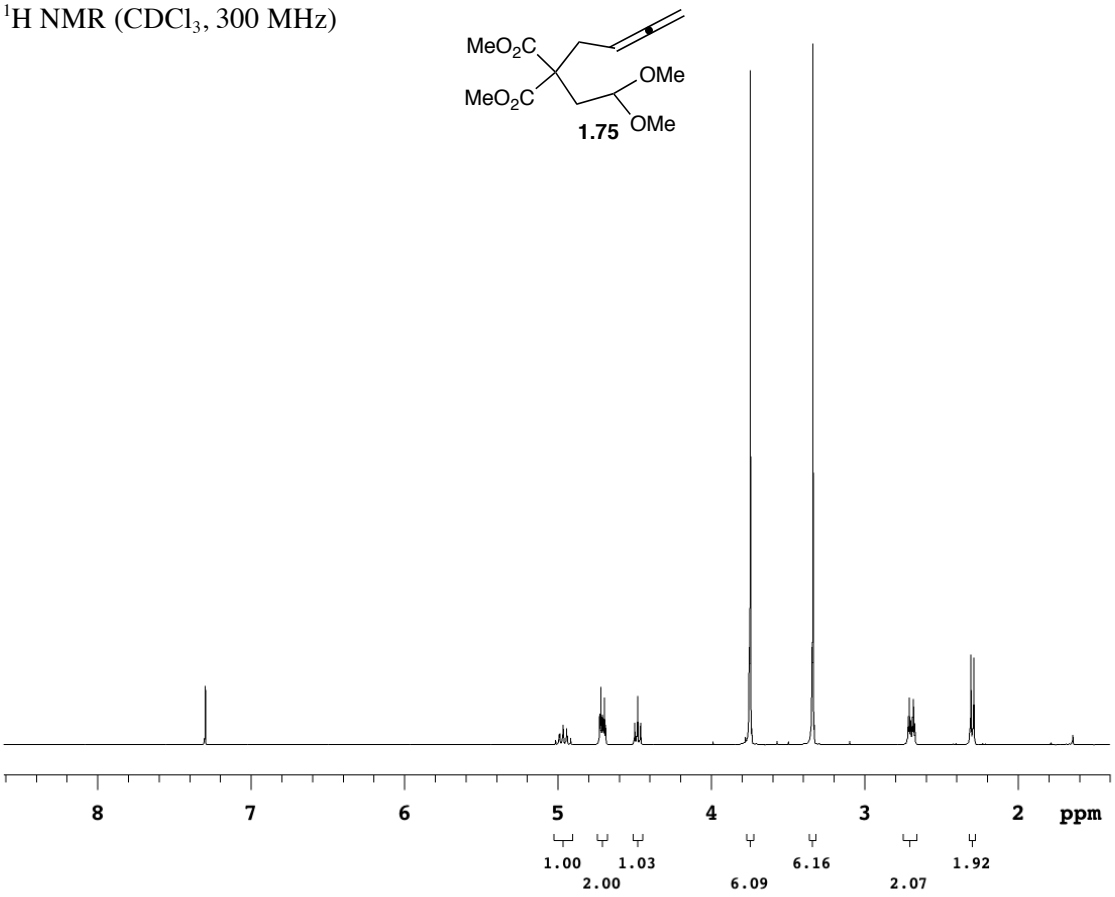

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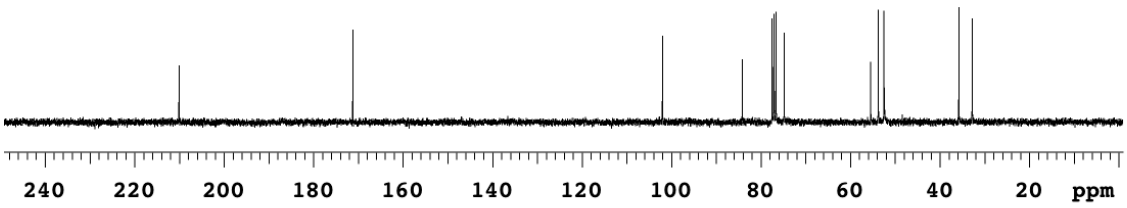

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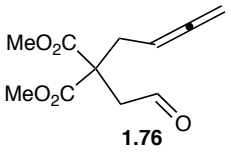

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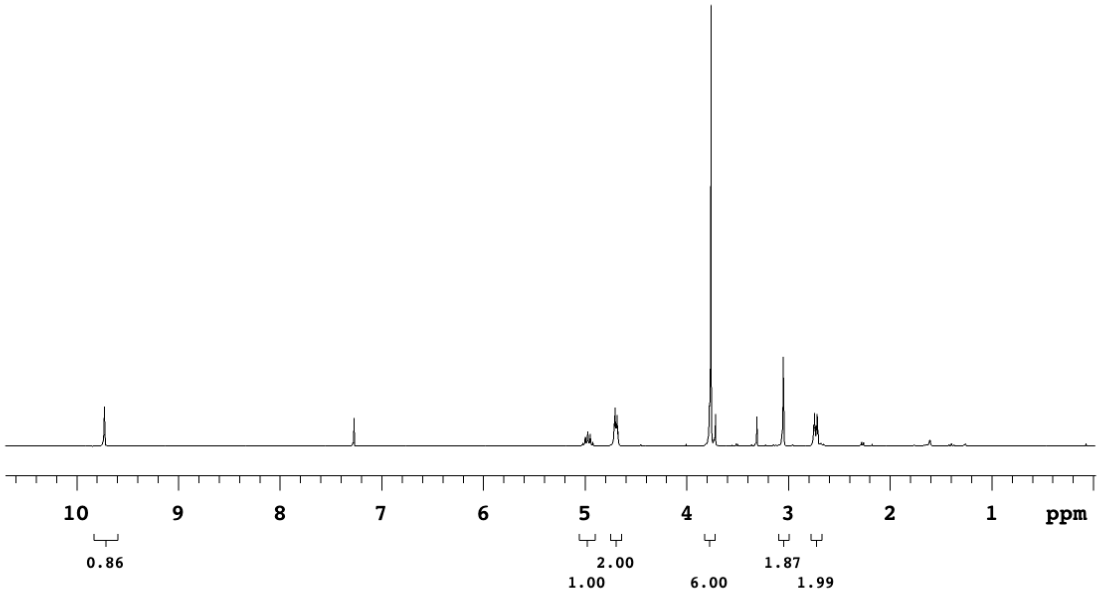

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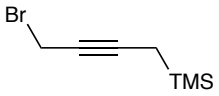

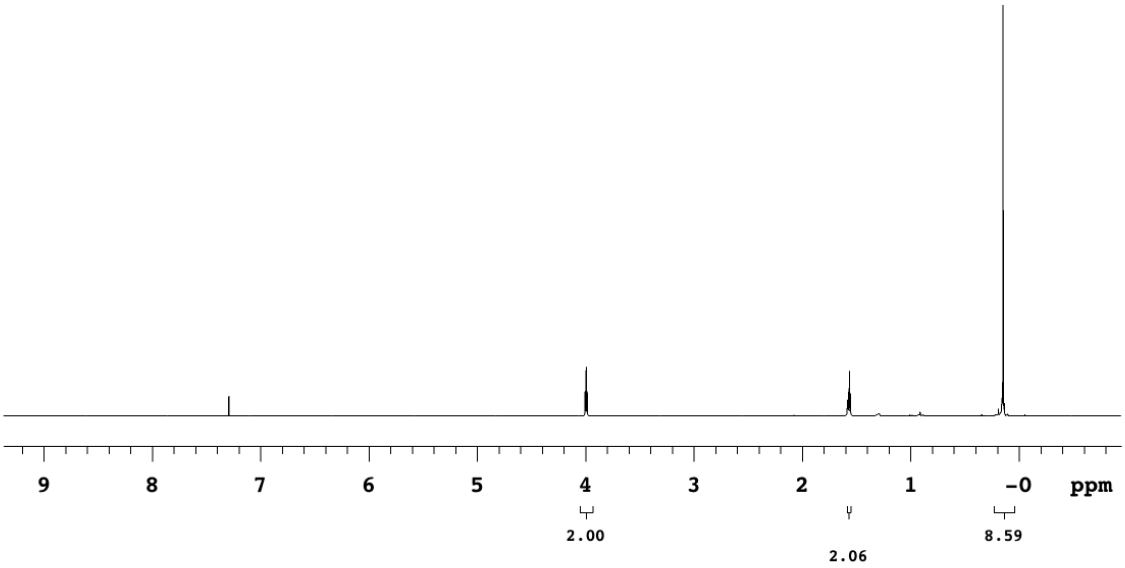

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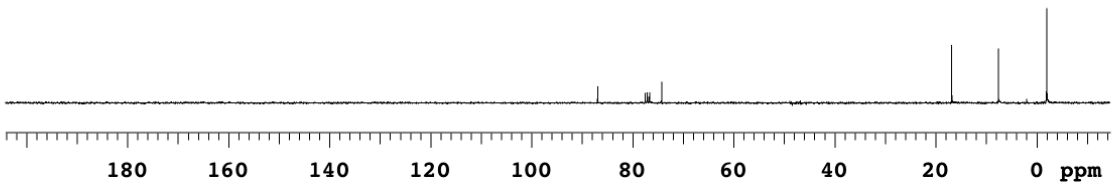

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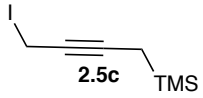

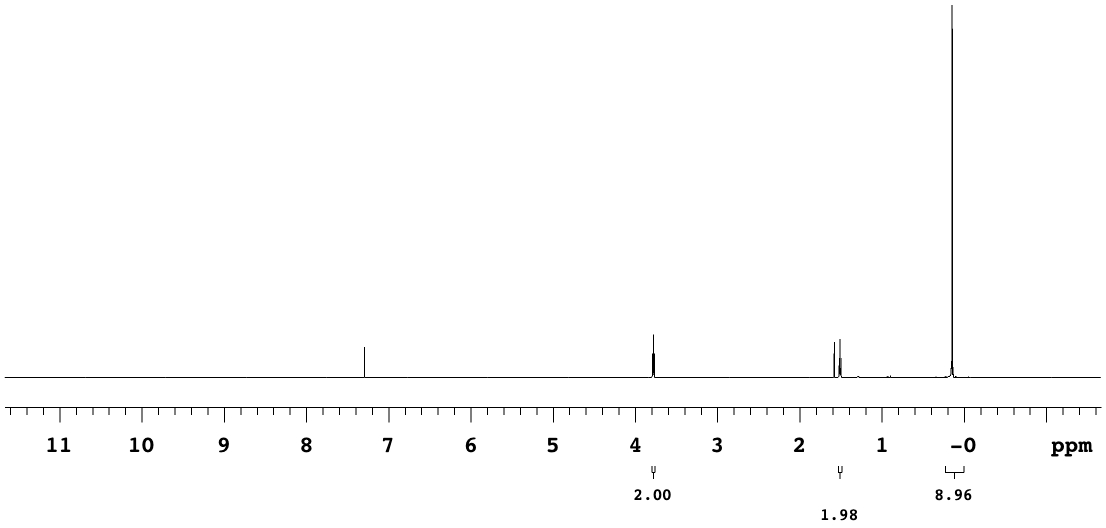

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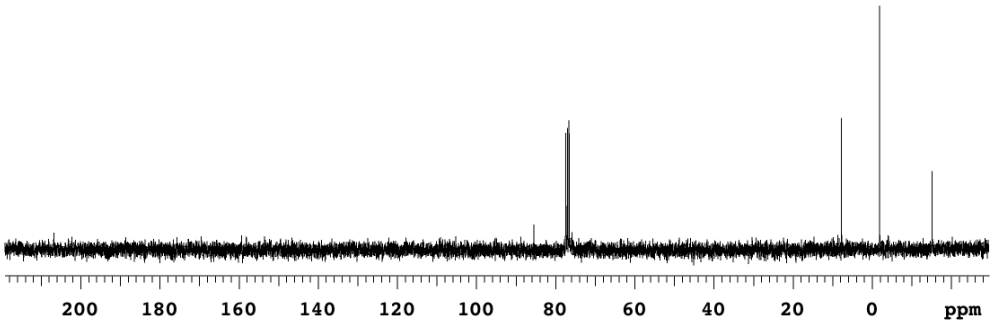

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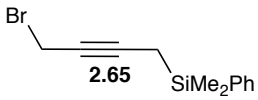

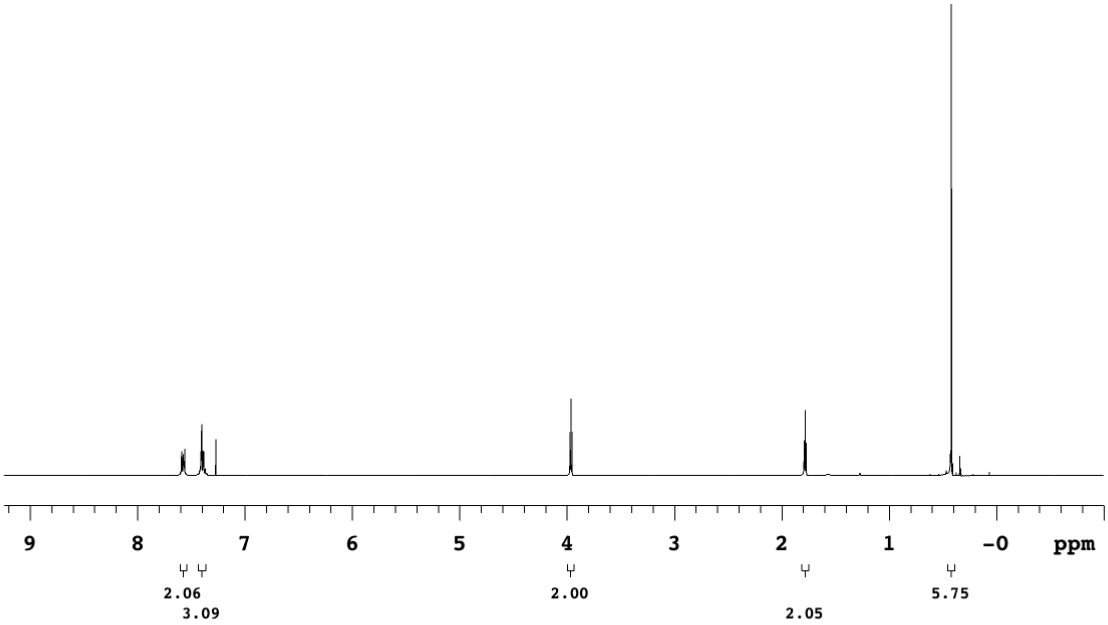

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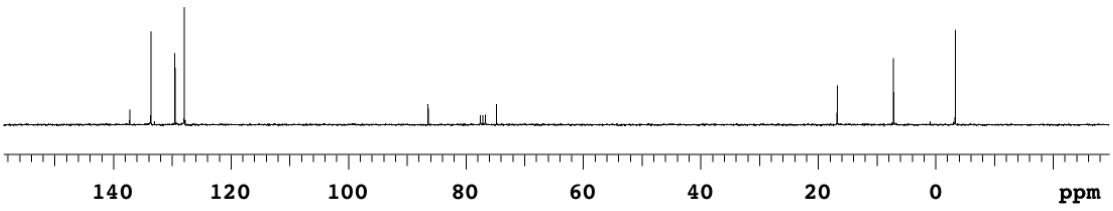

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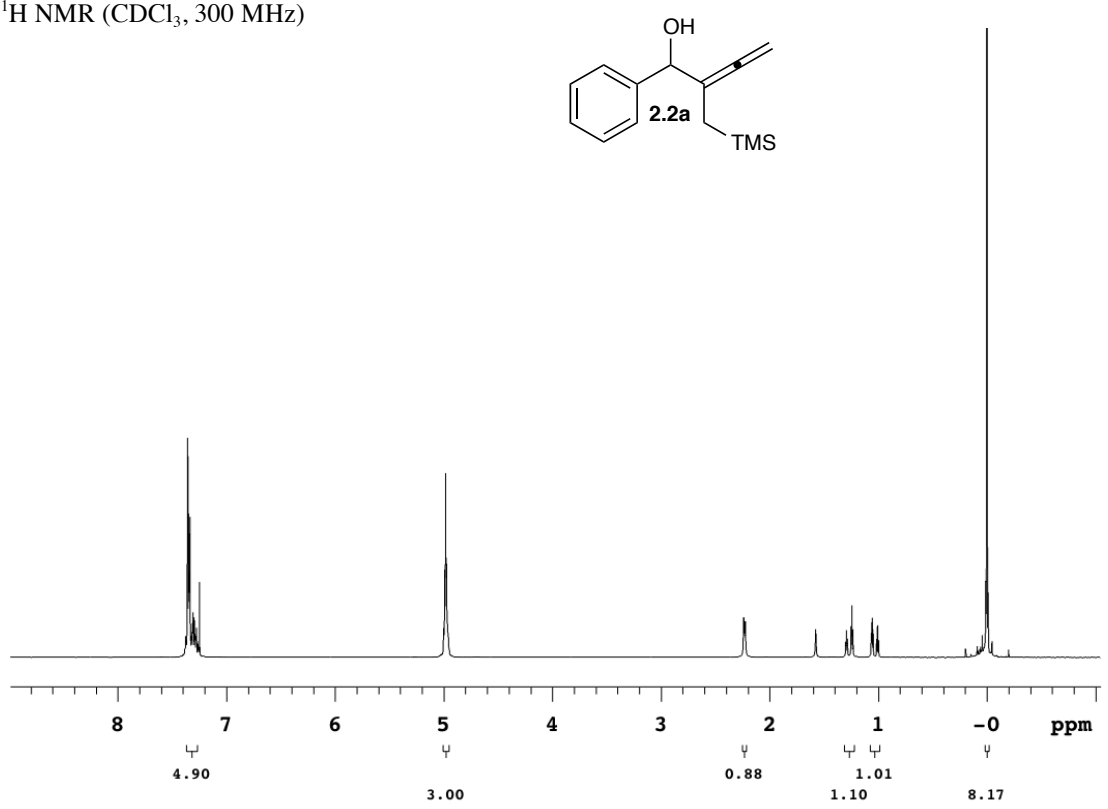

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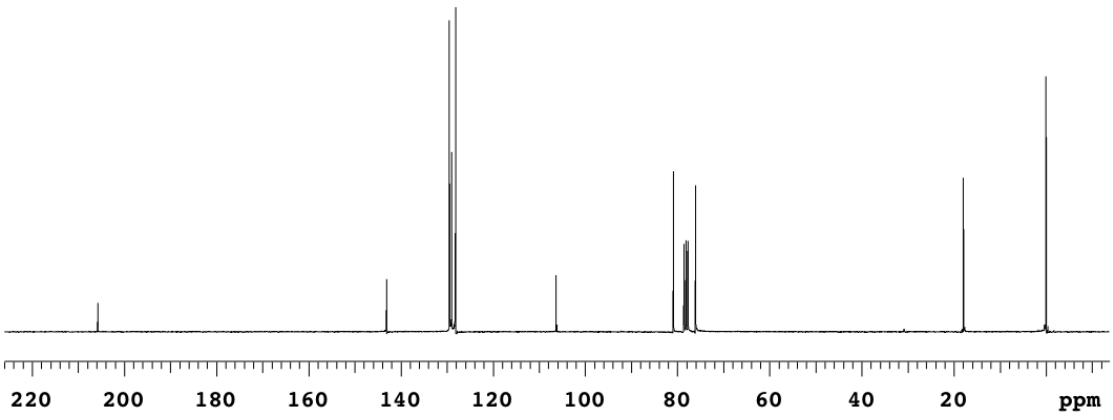
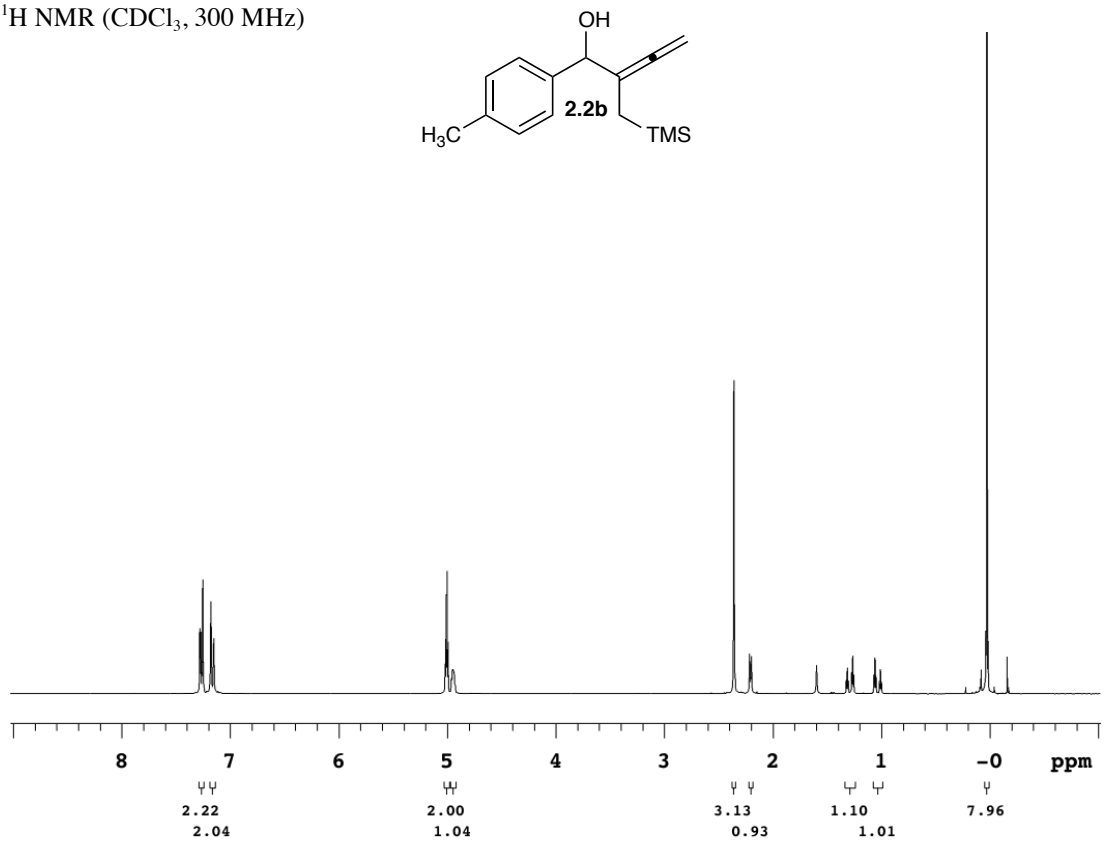
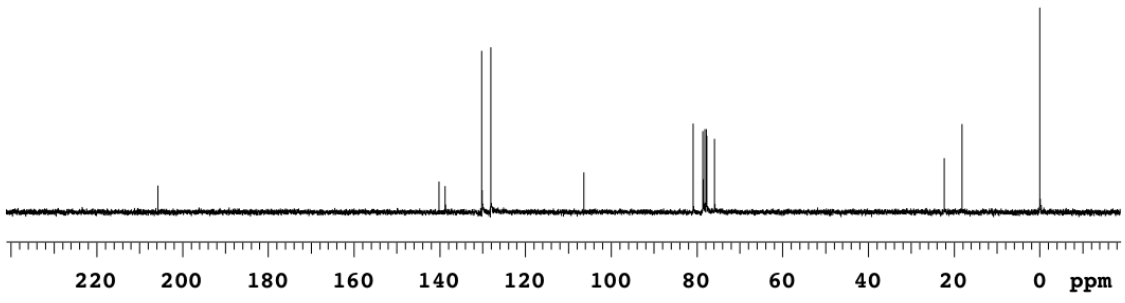


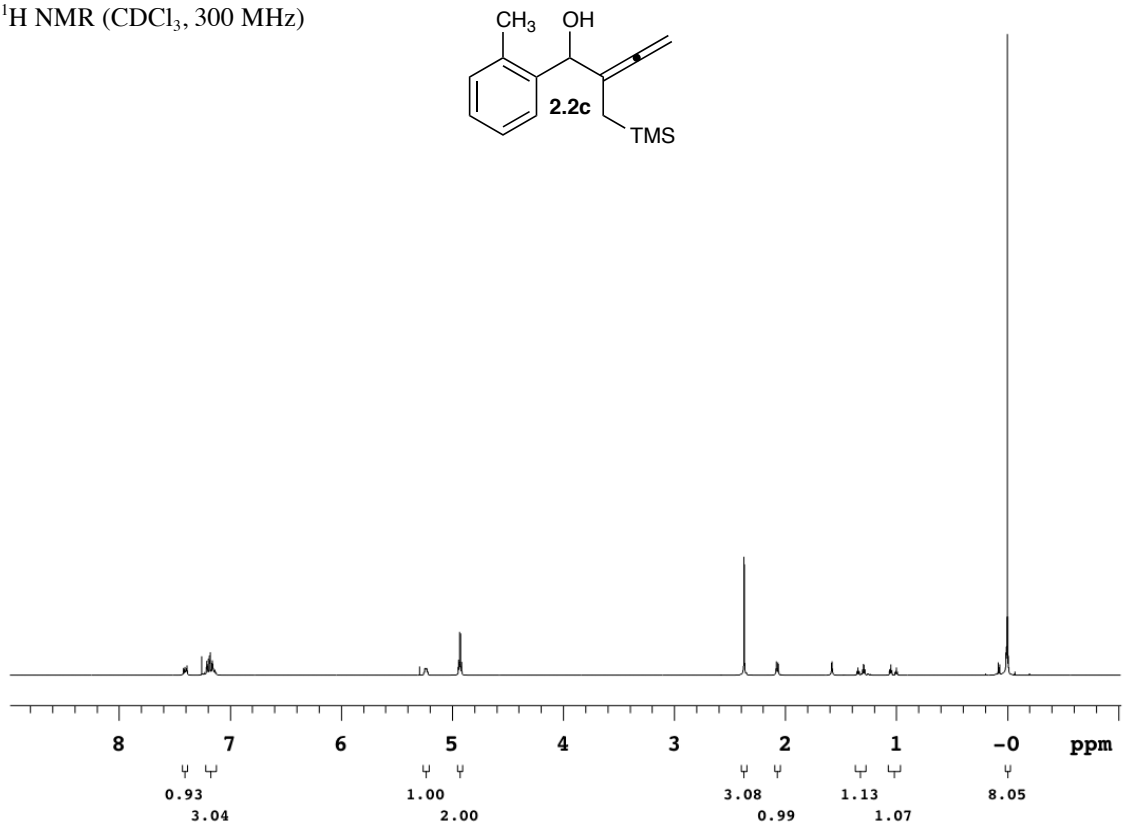
^{1}H NMR ($CDCl_3$, 300 MHz)



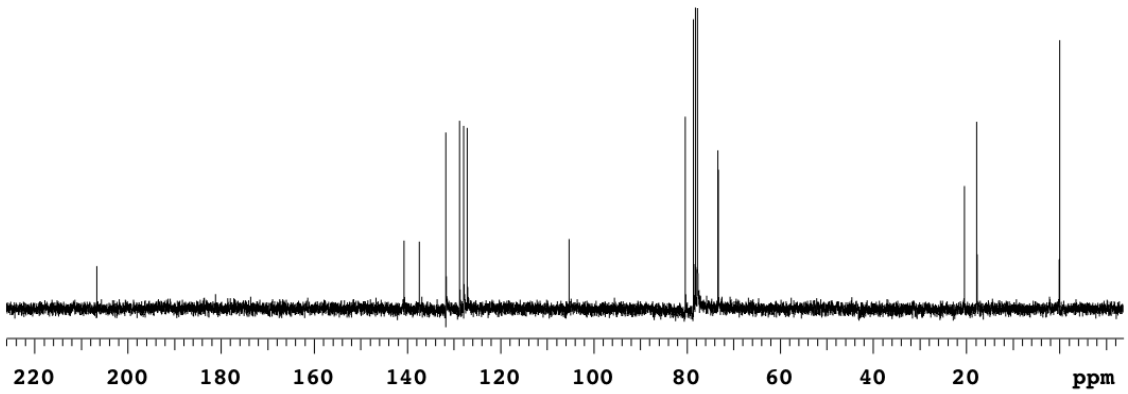
^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



^{13}C NMR ($CDCl_3$, 75 MHz)



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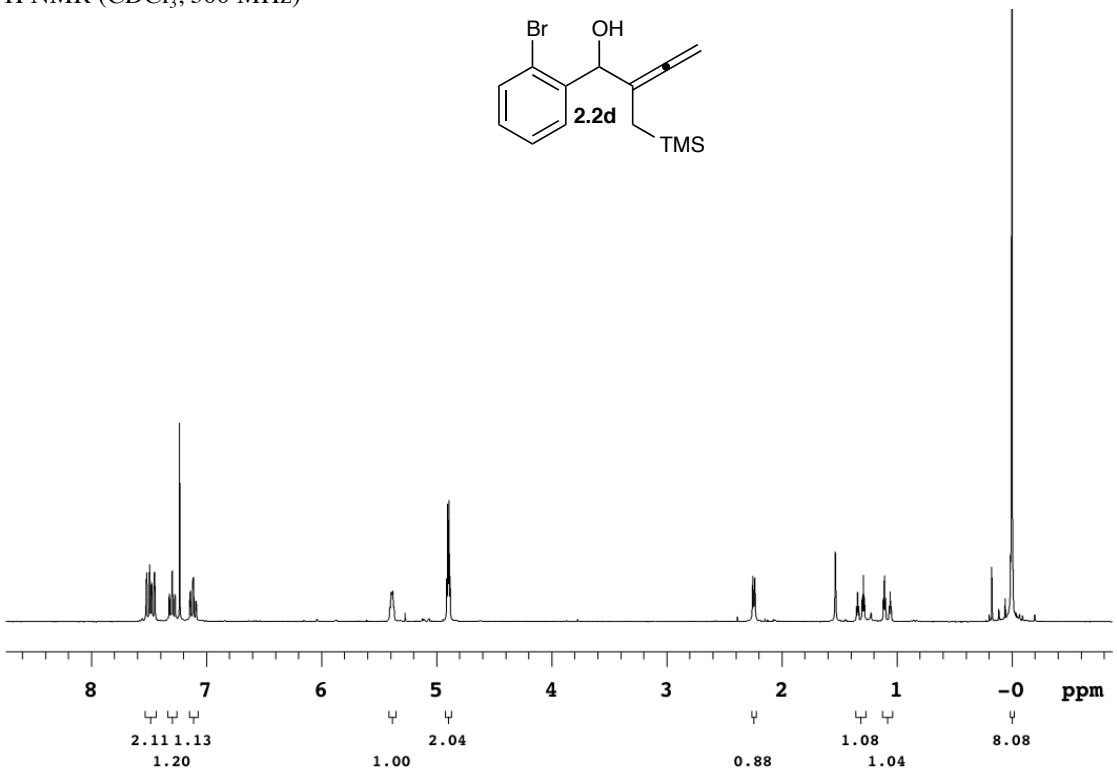

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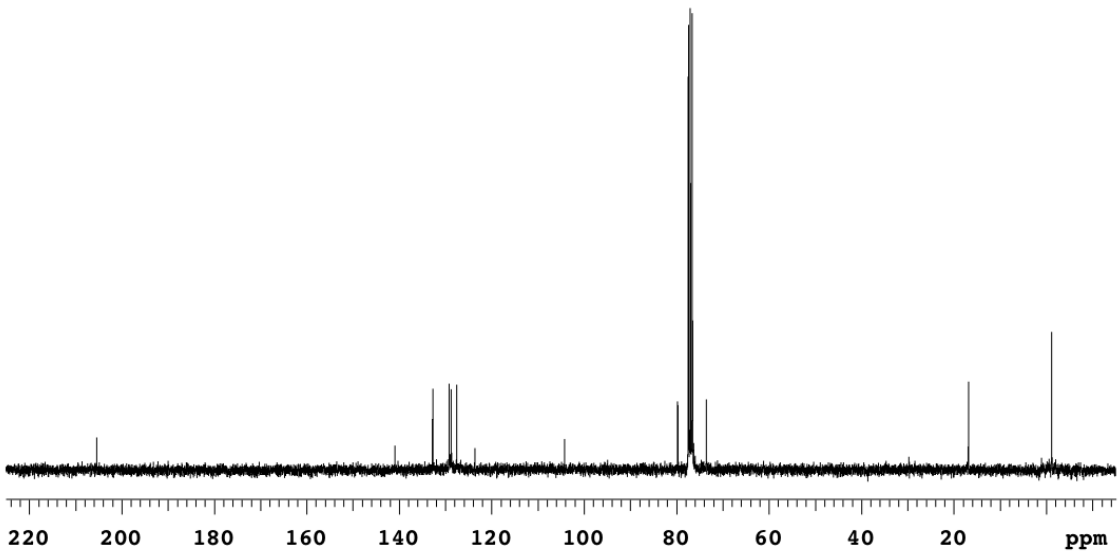

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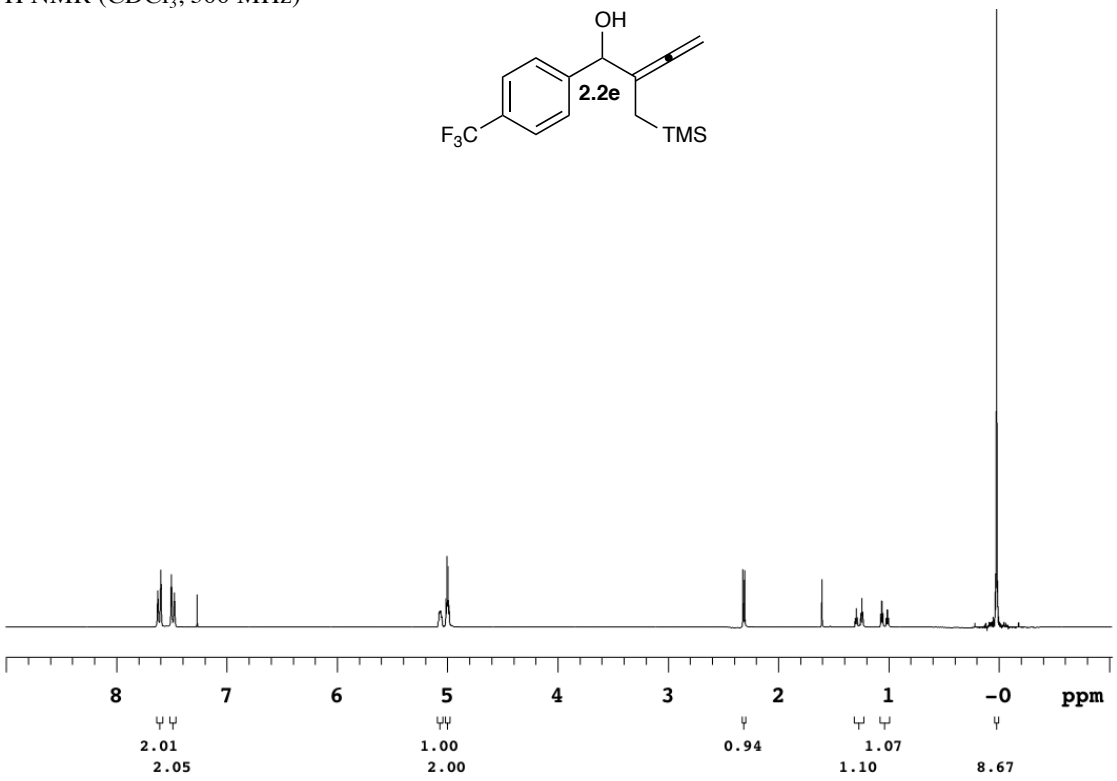

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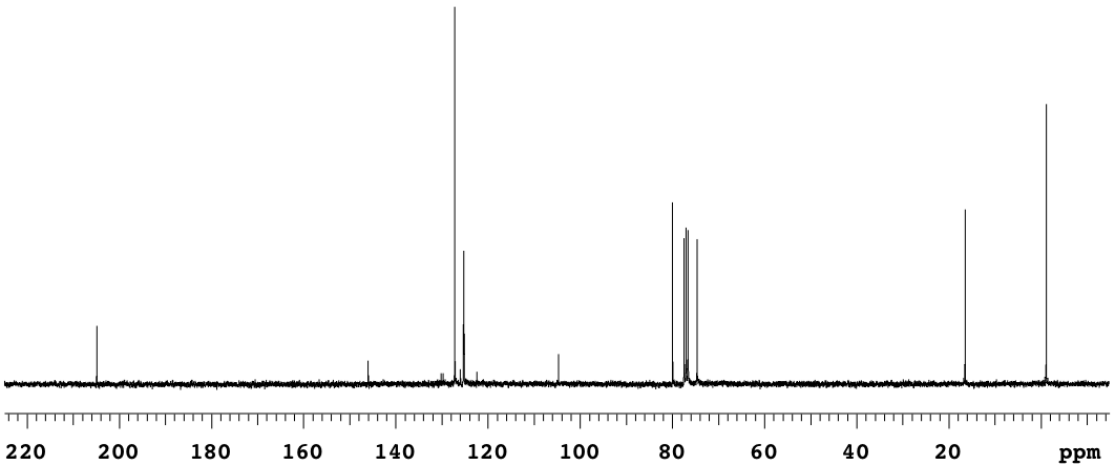

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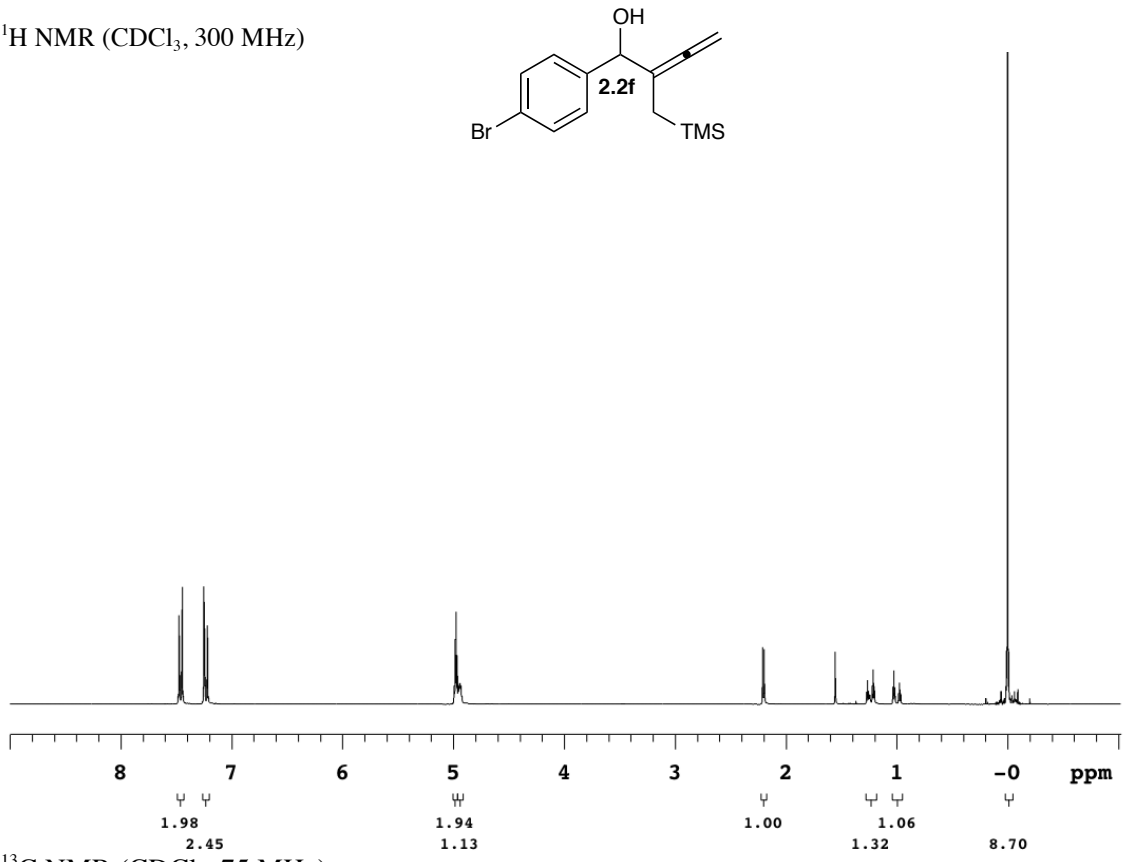

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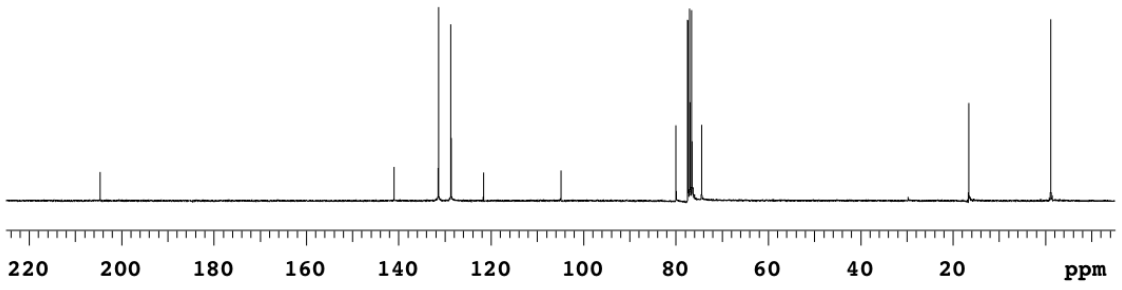

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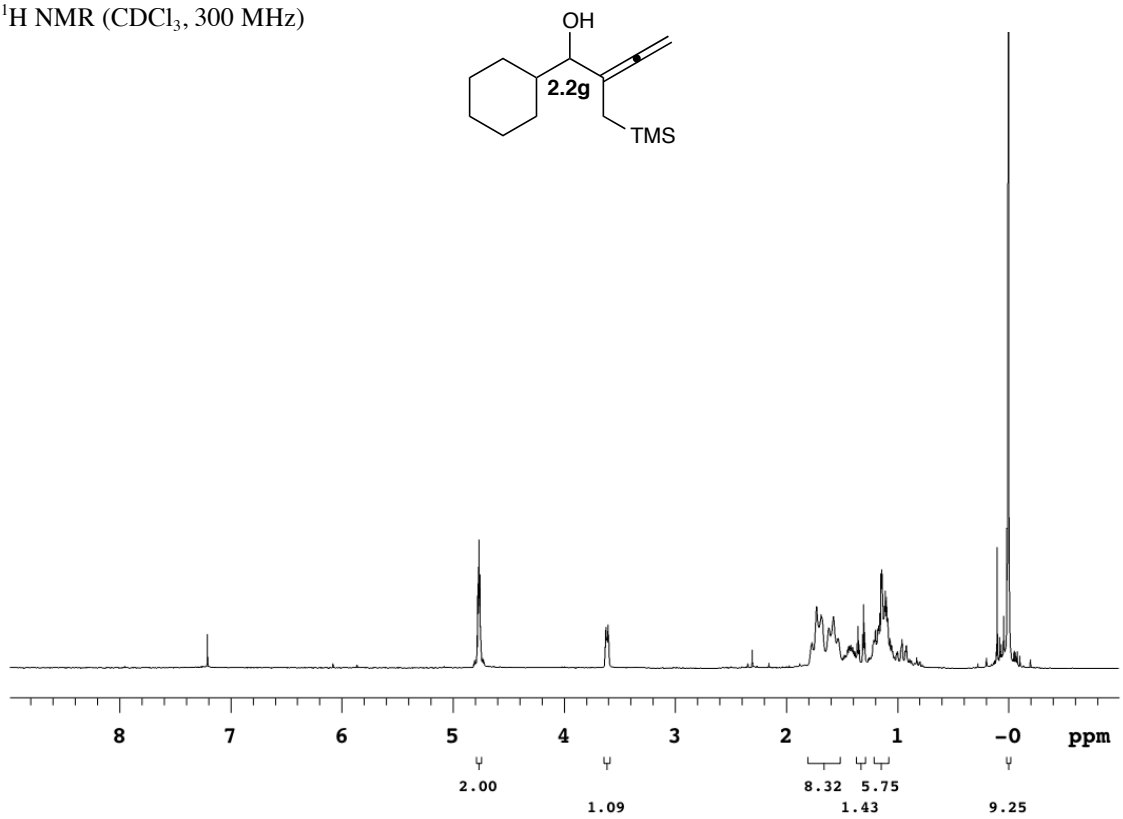

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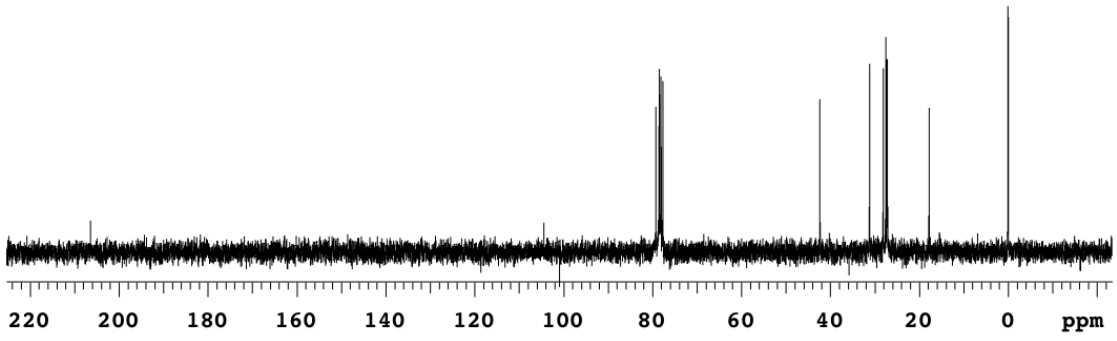

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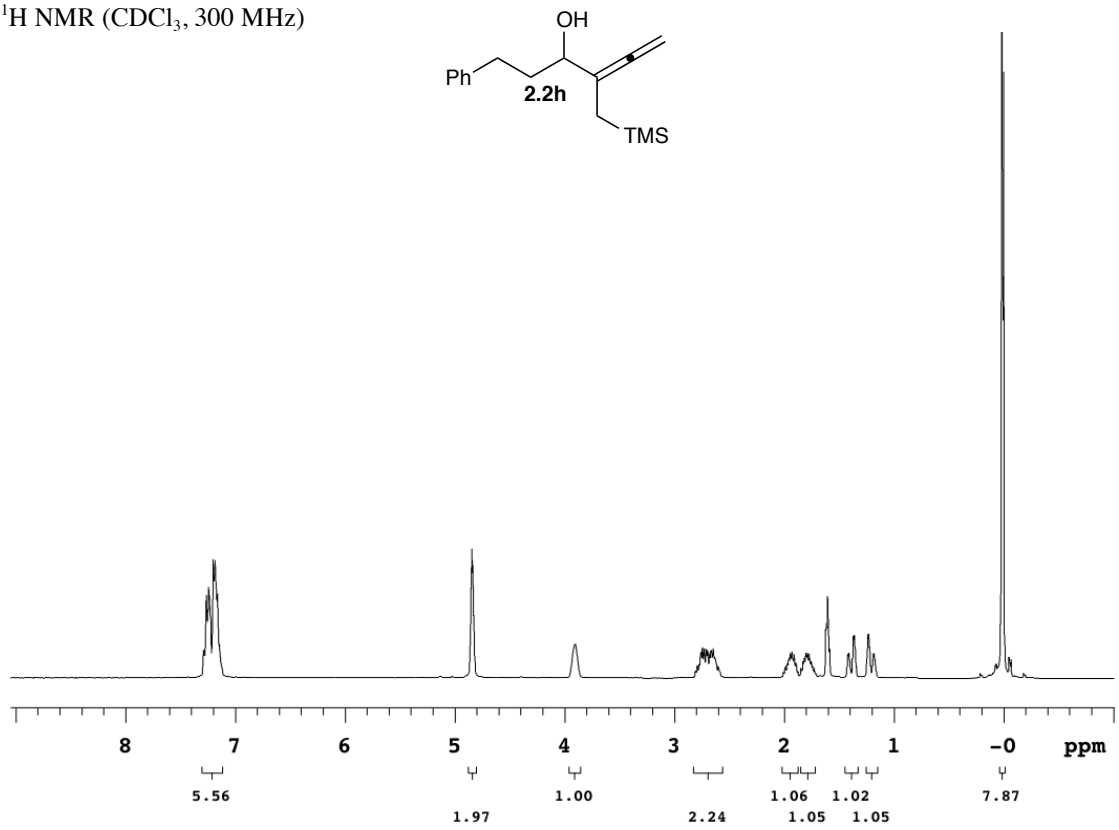

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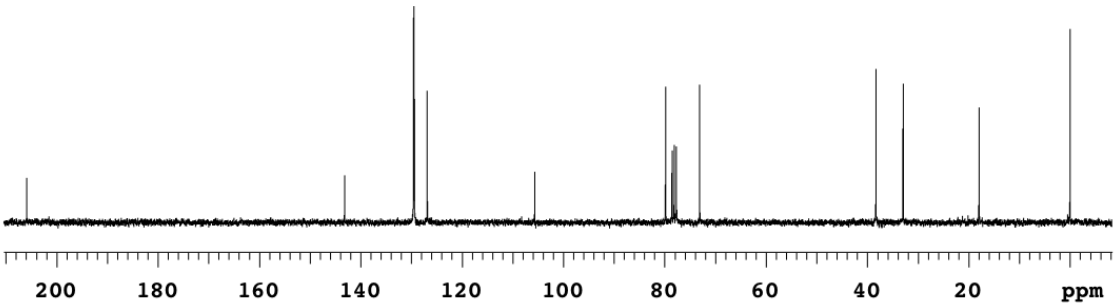

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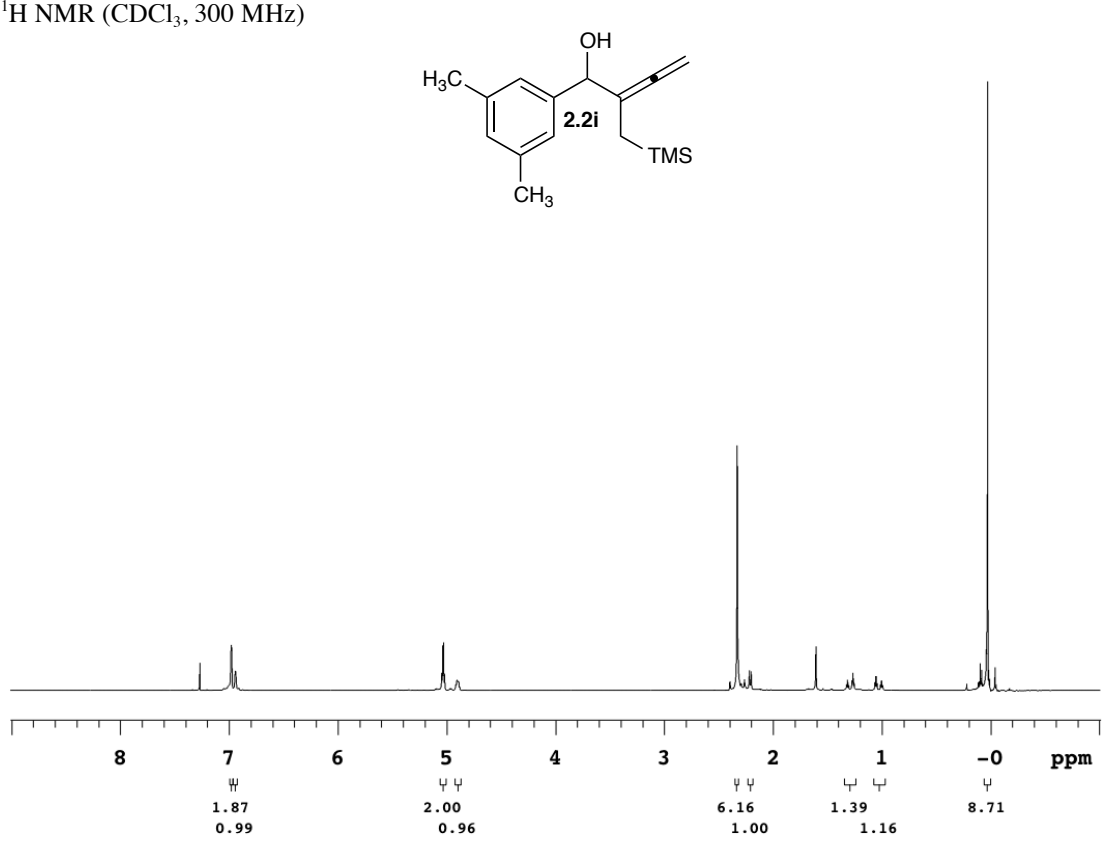

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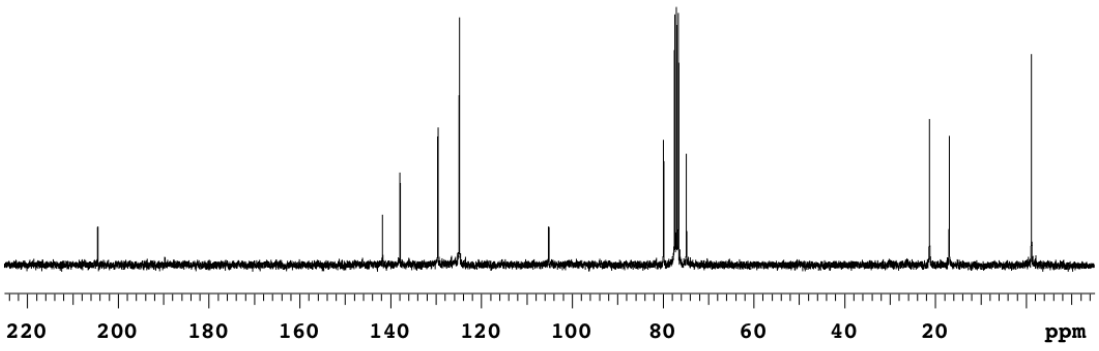

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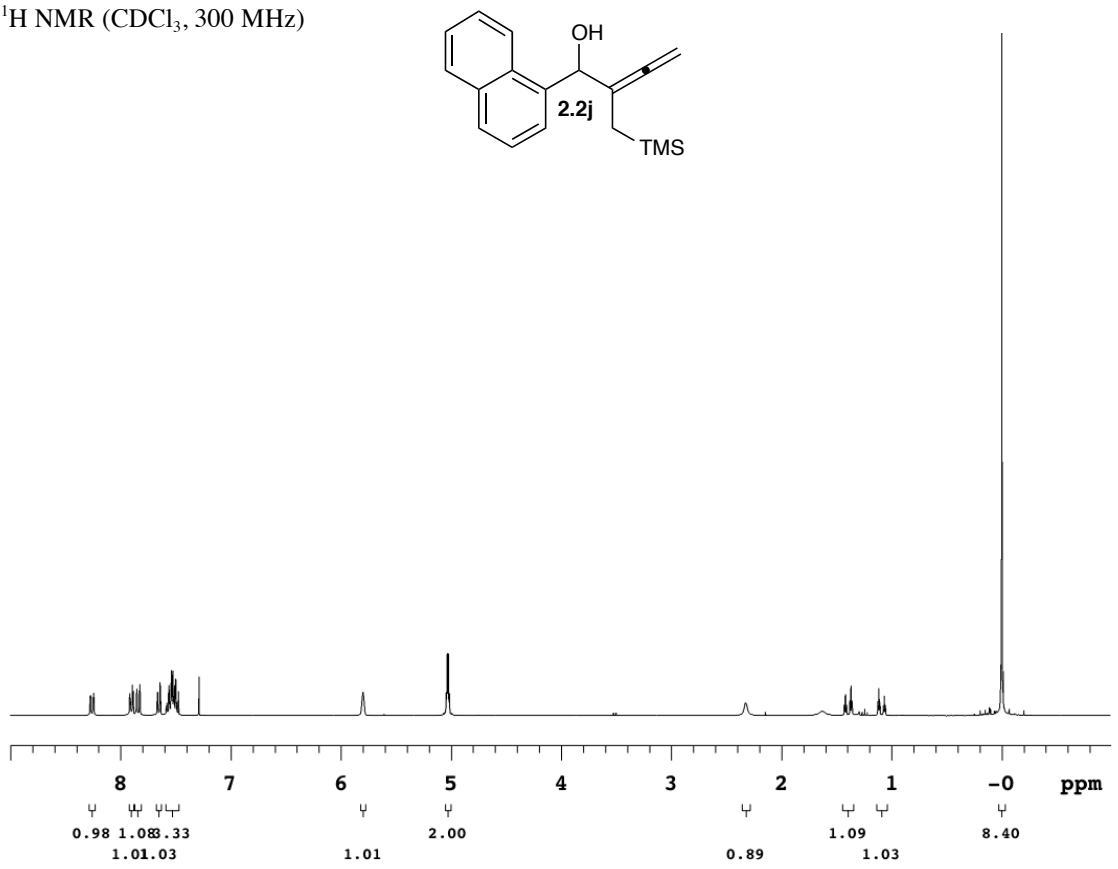

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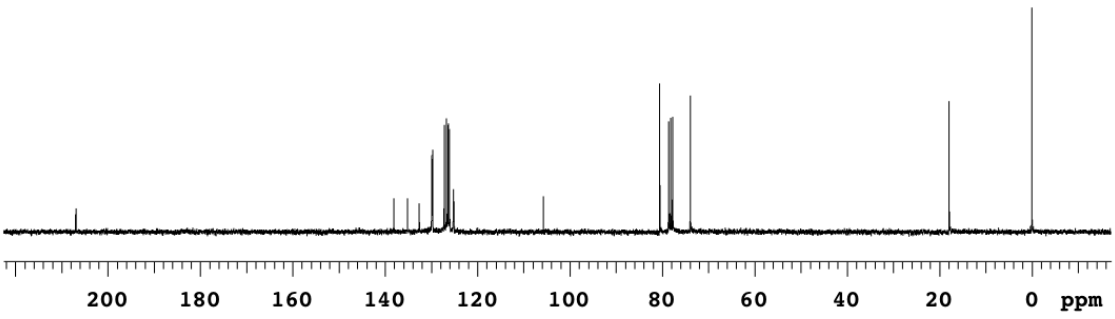

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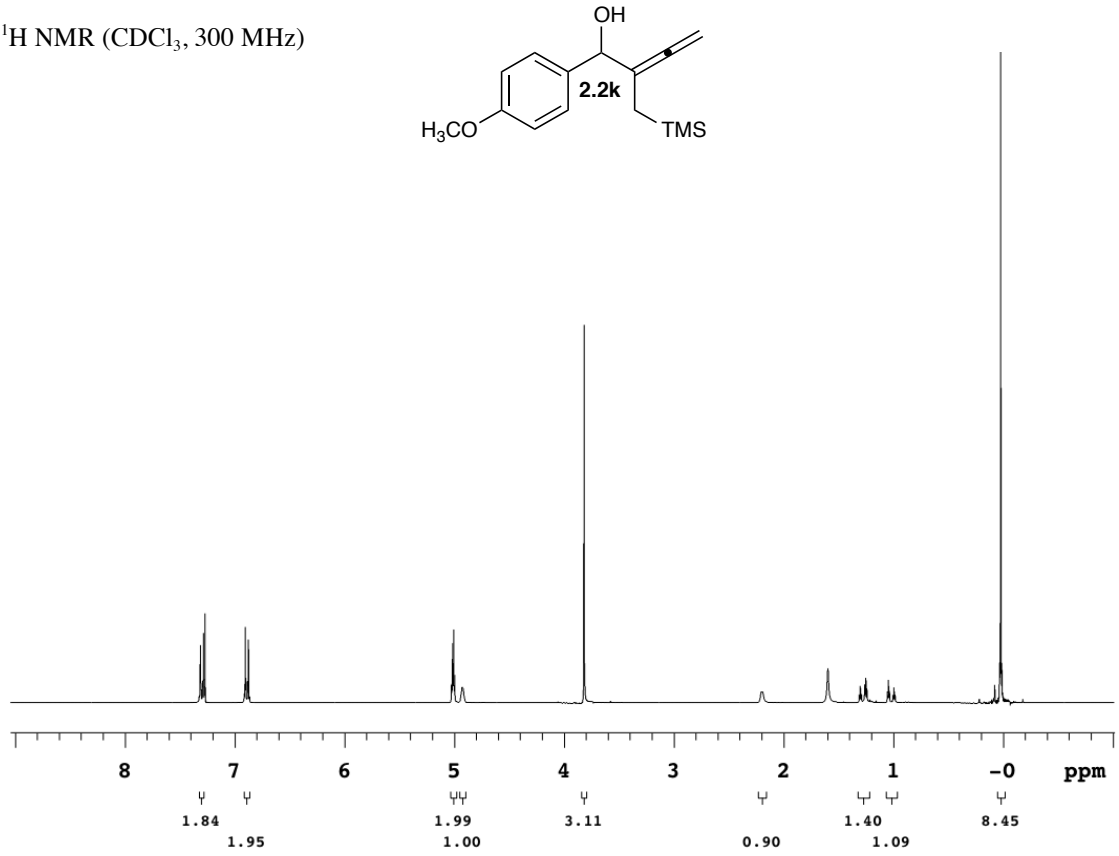

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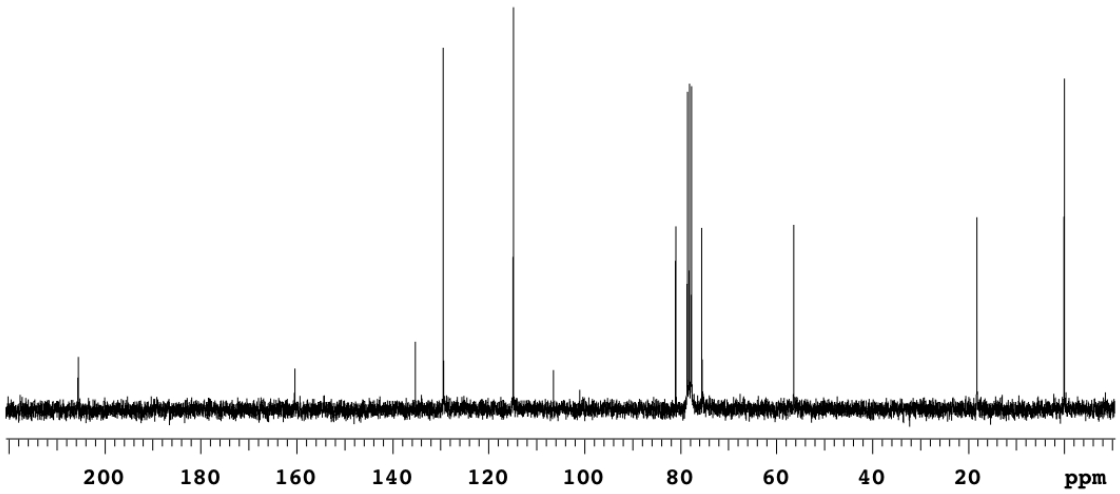

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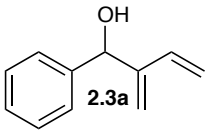

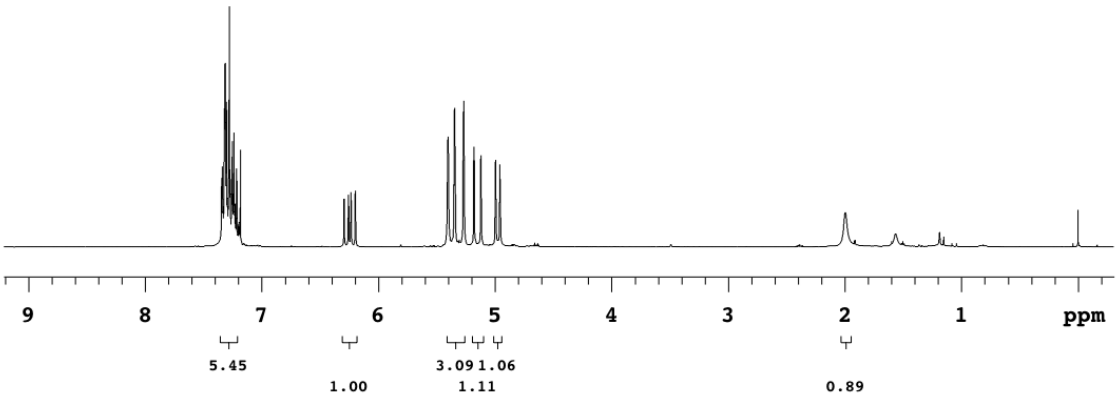

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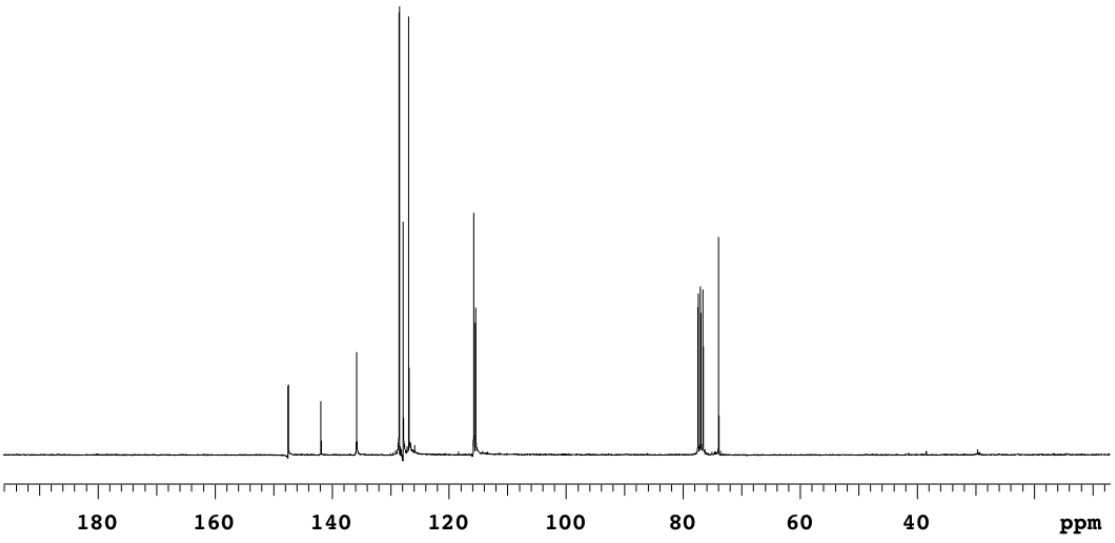

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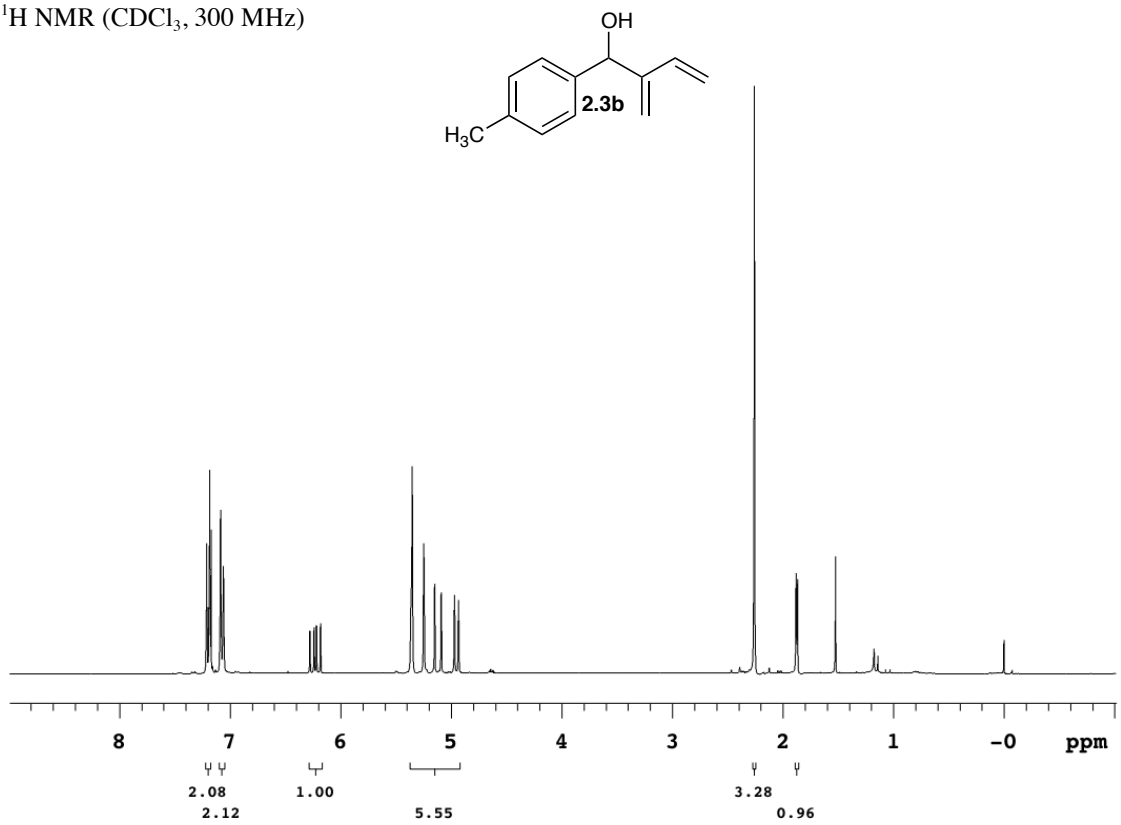

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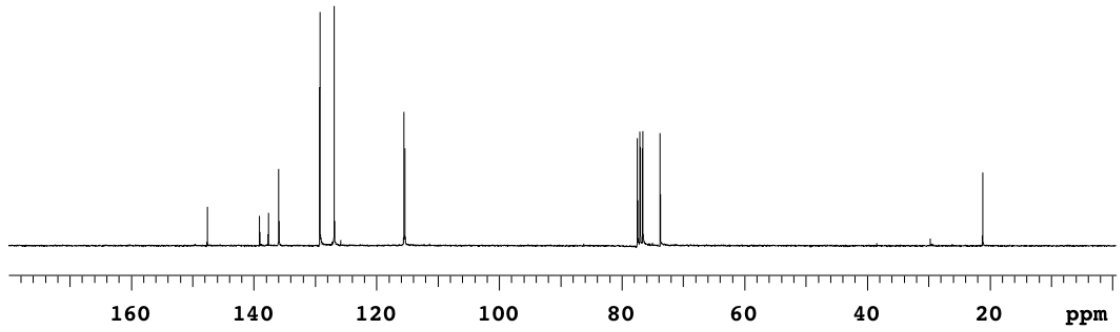

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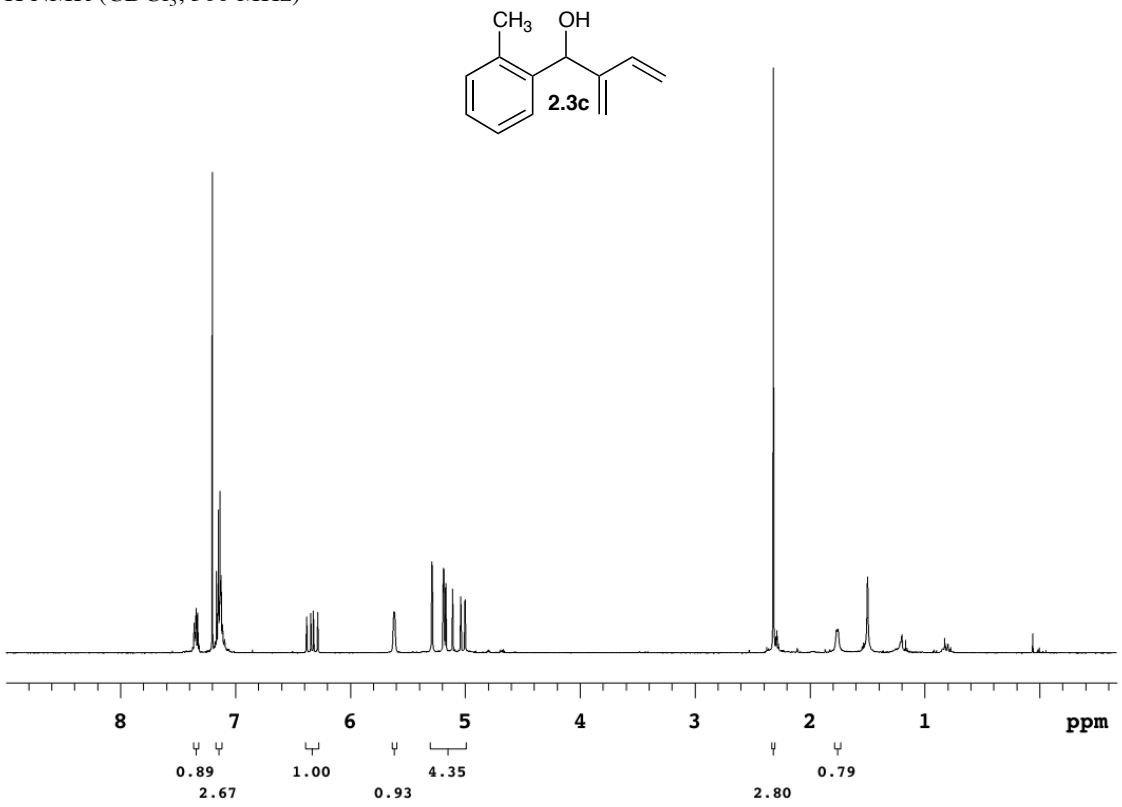

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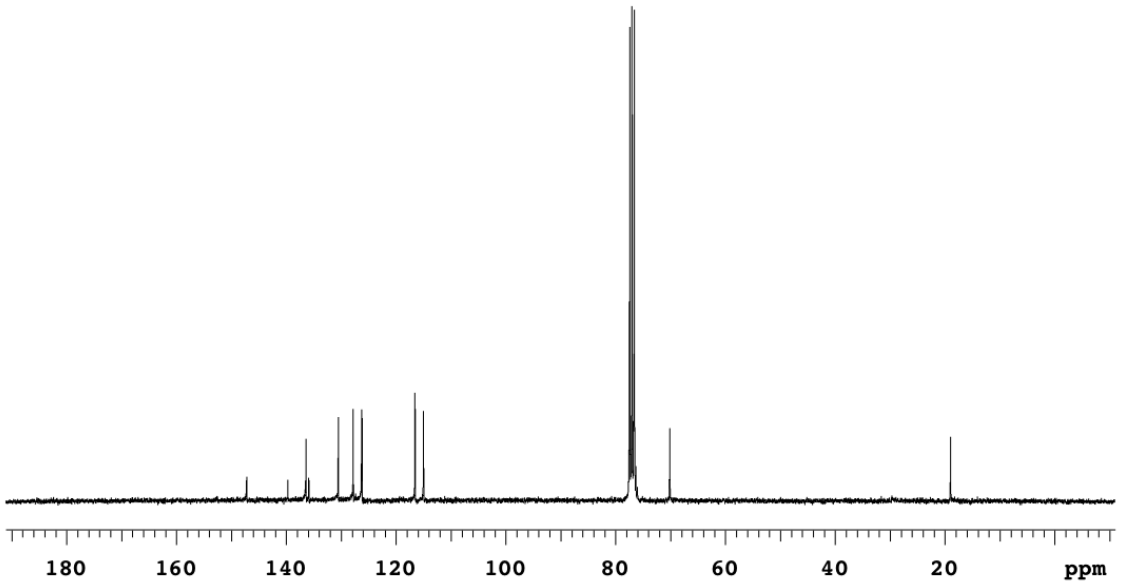

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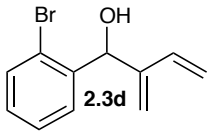

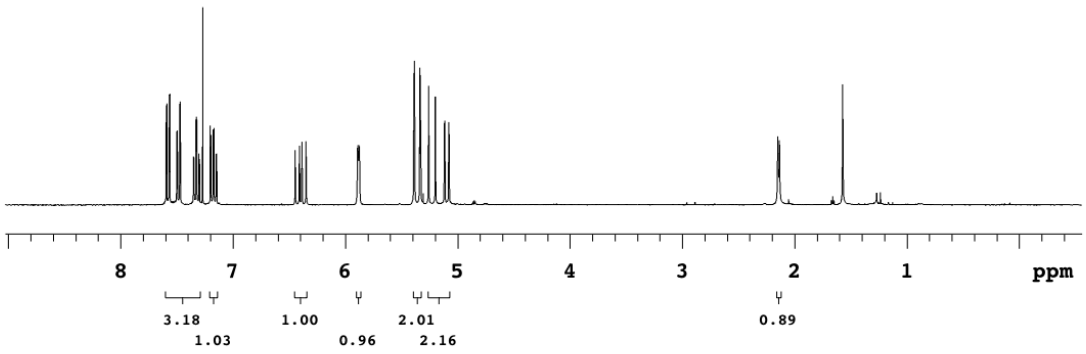

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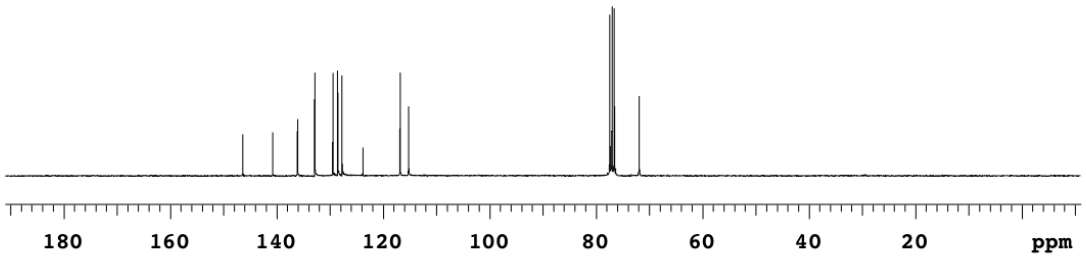

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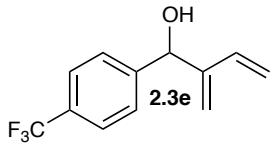

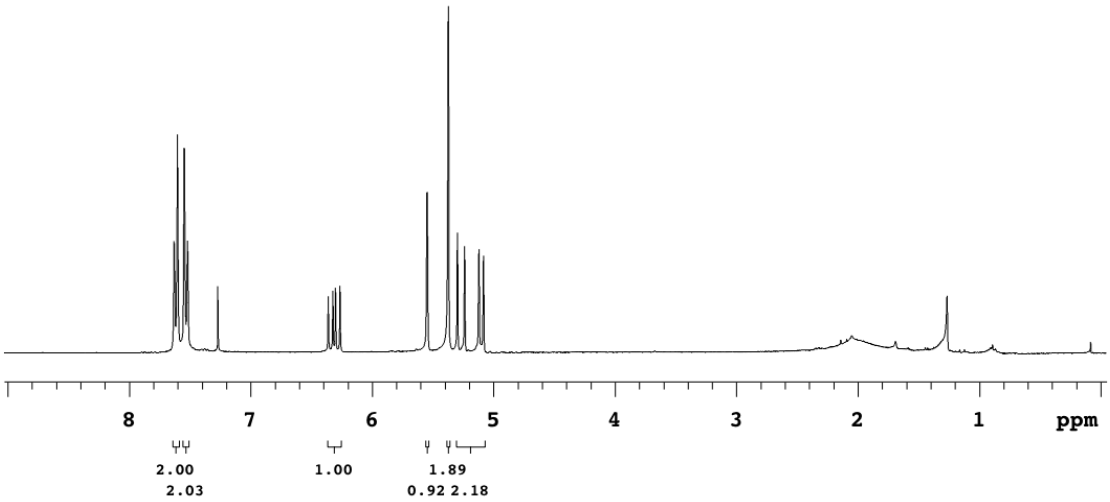

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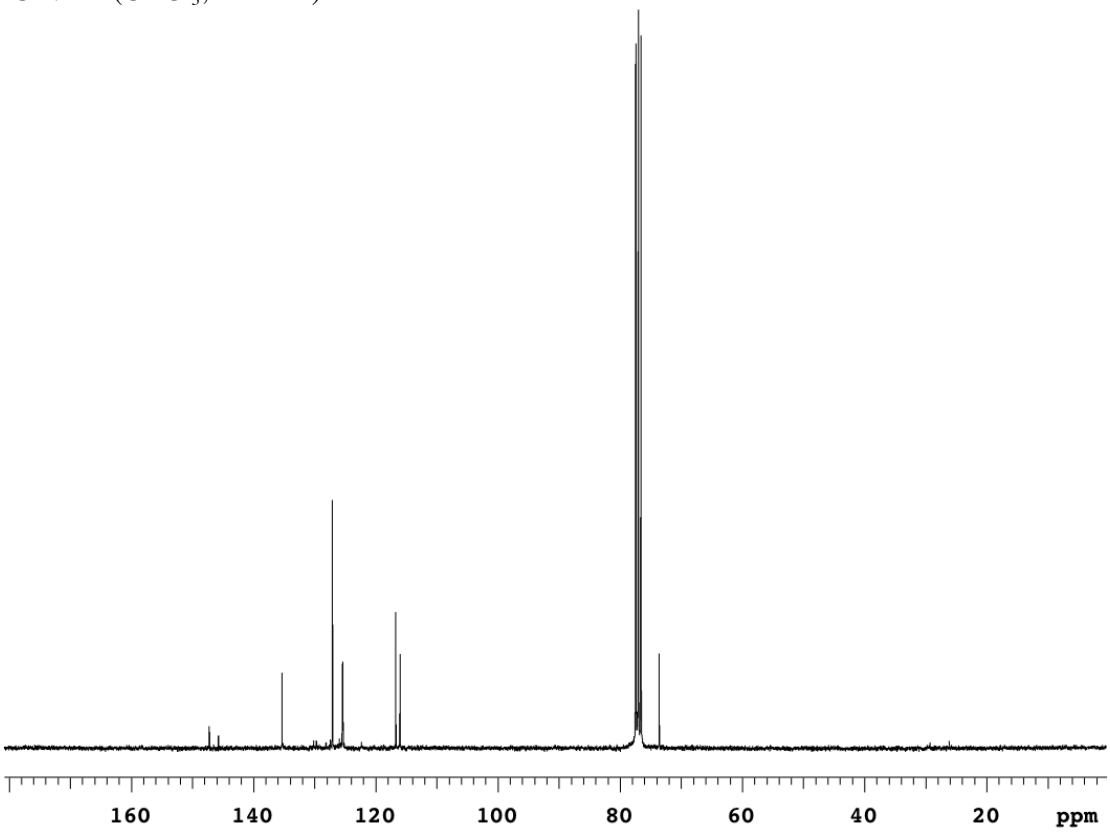

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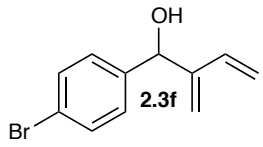

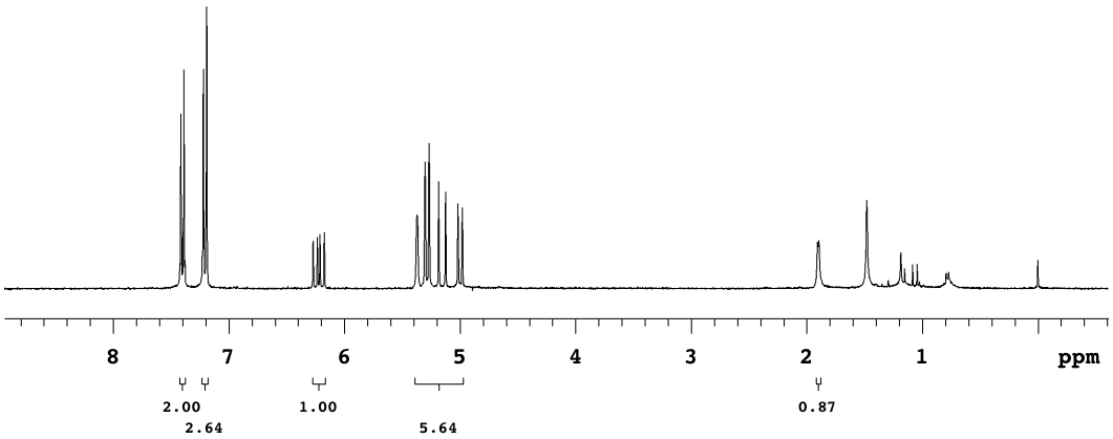

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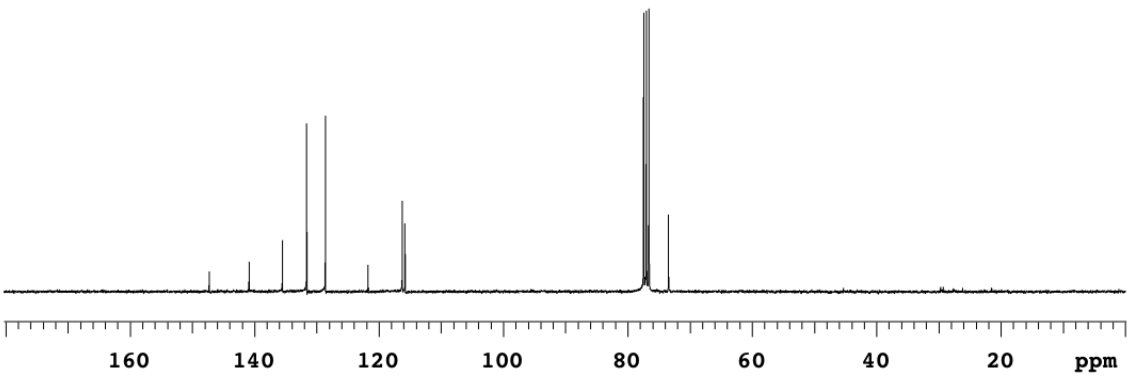

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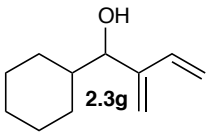

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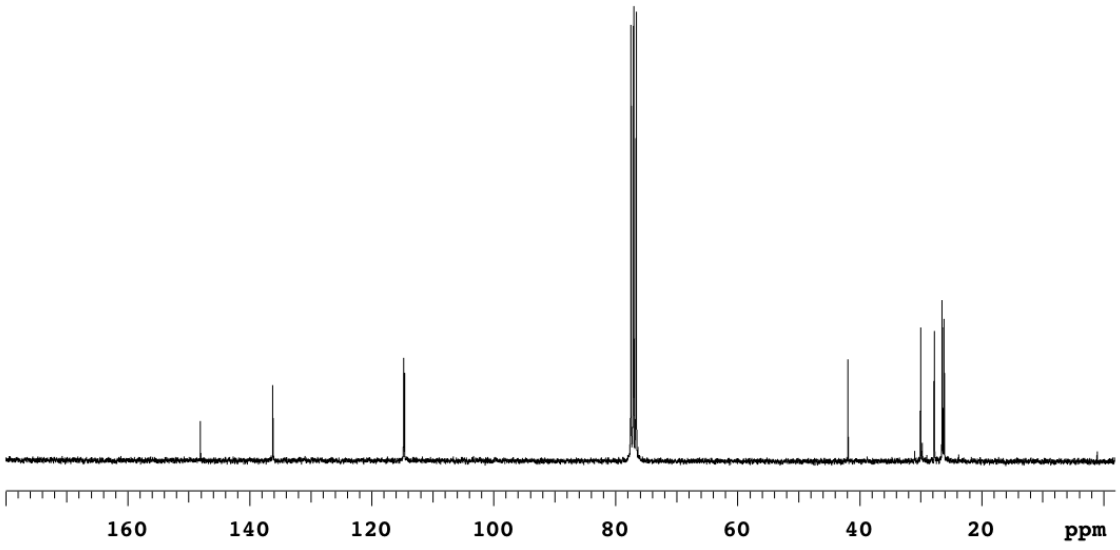

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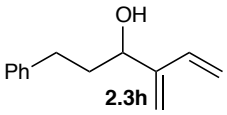

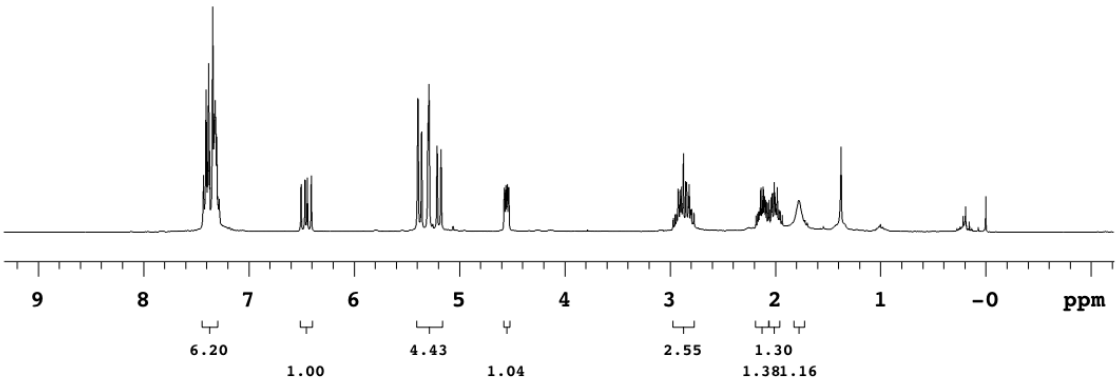

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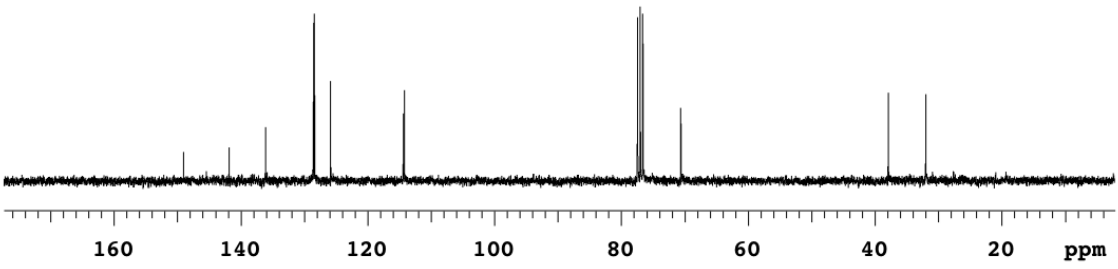

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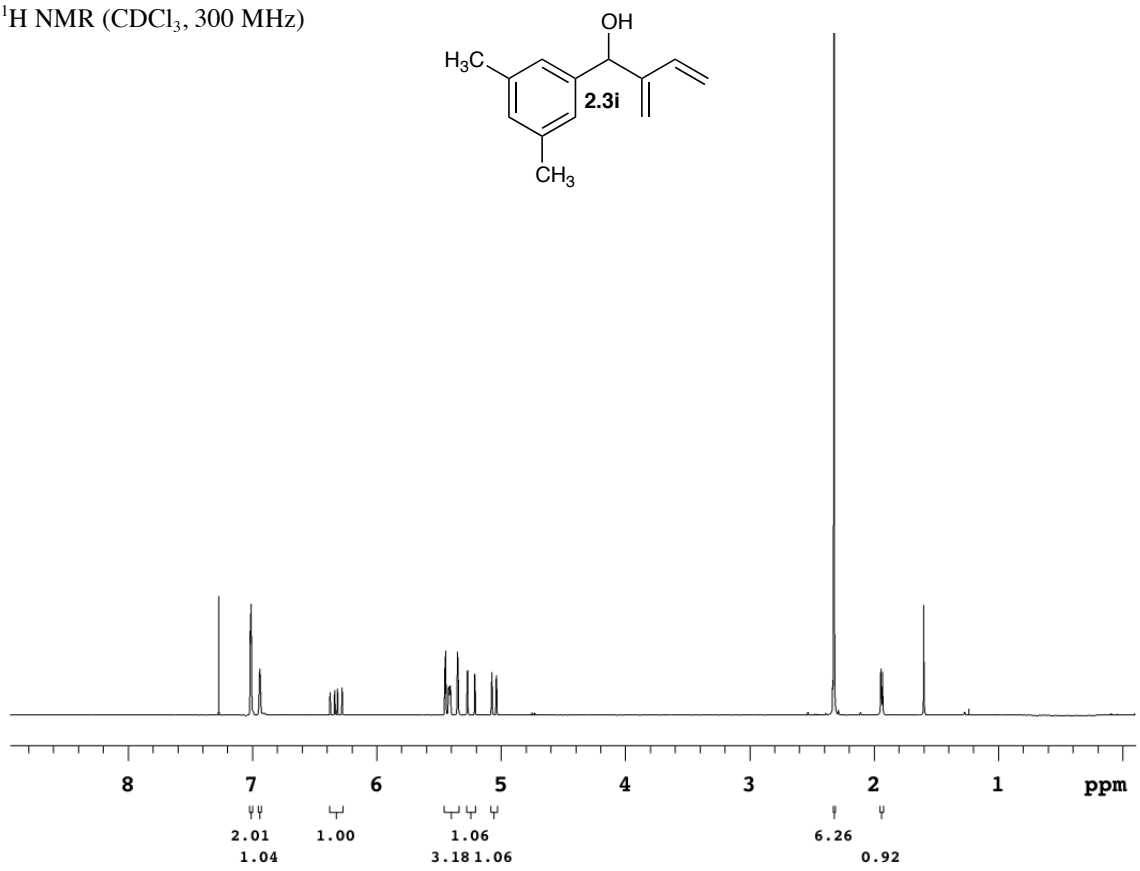

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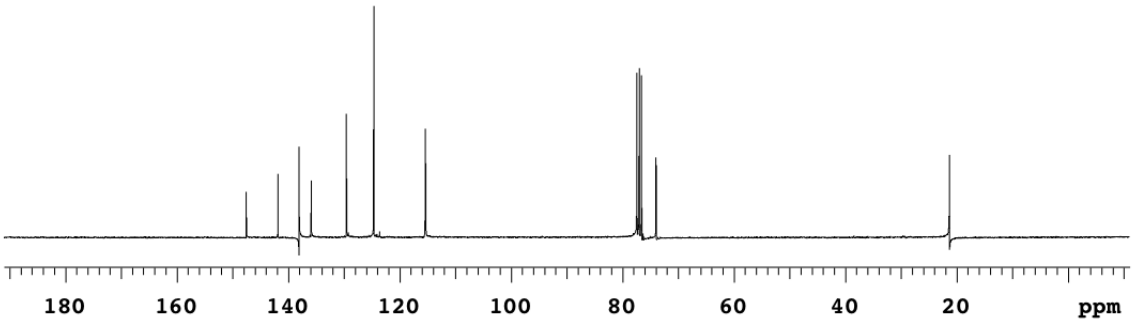

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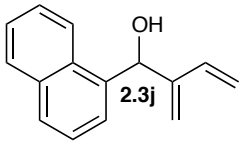

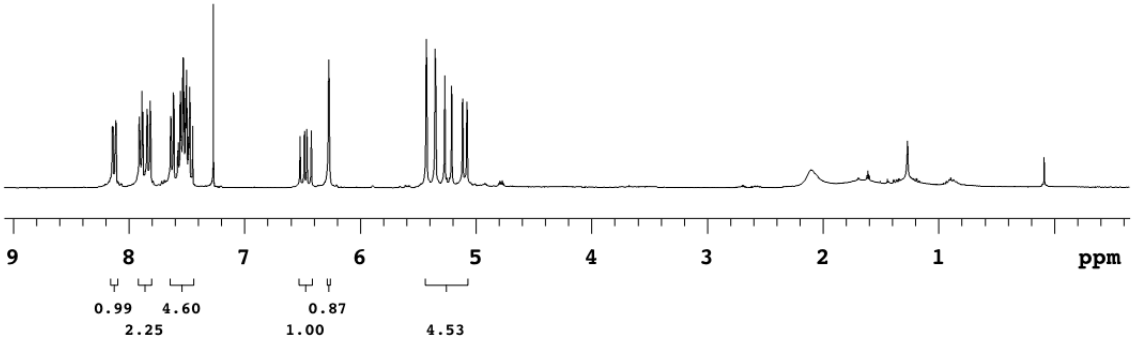

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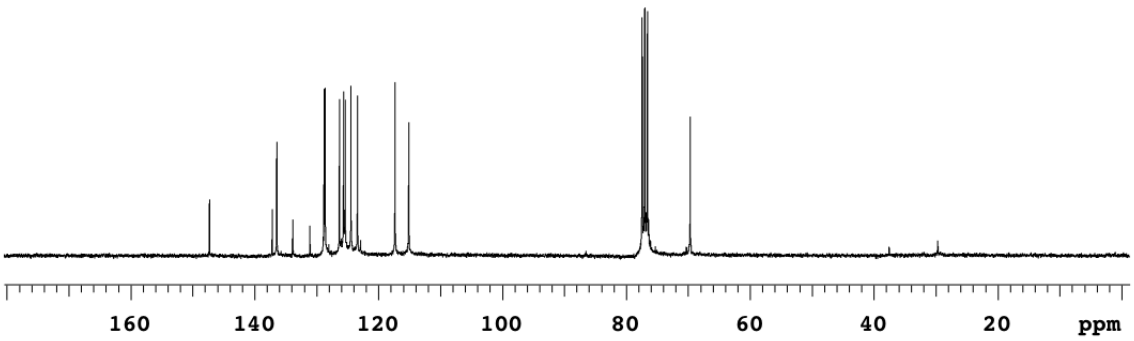

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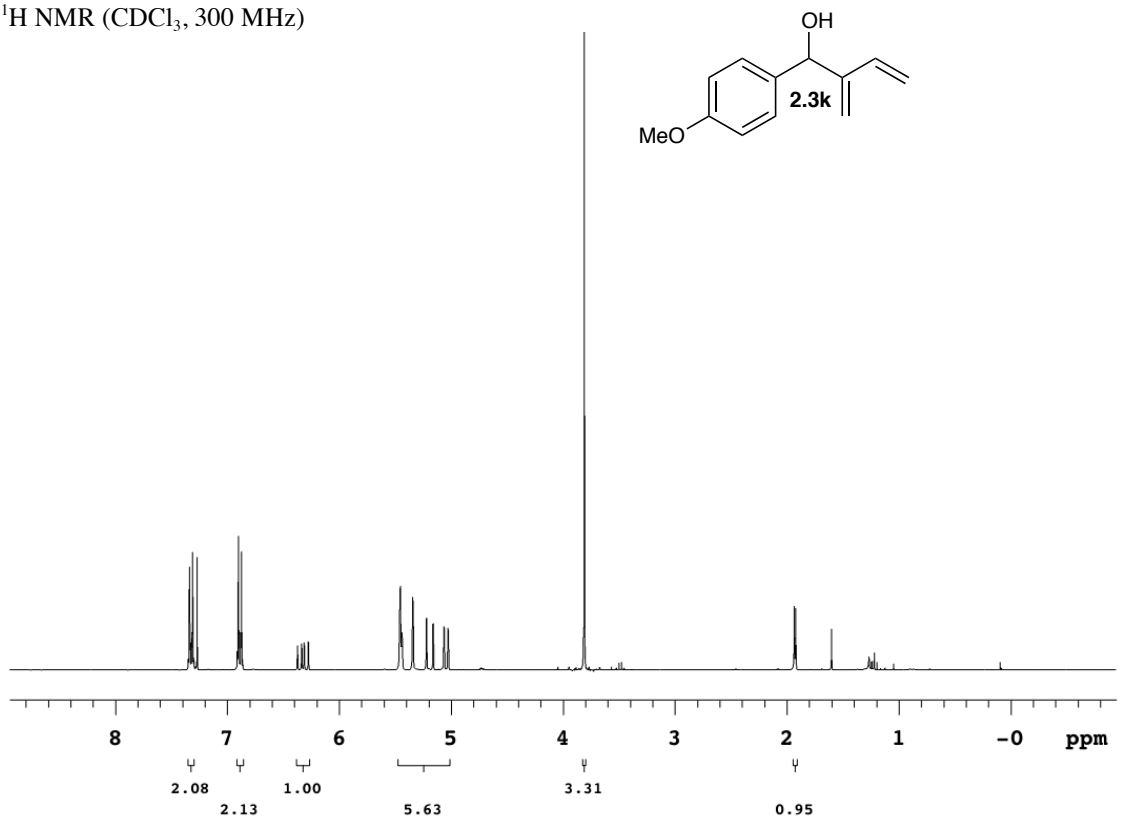

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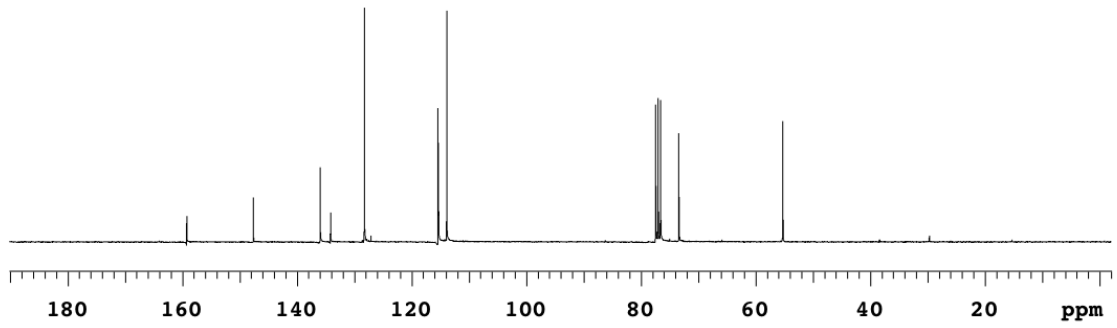

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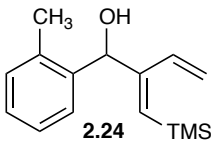
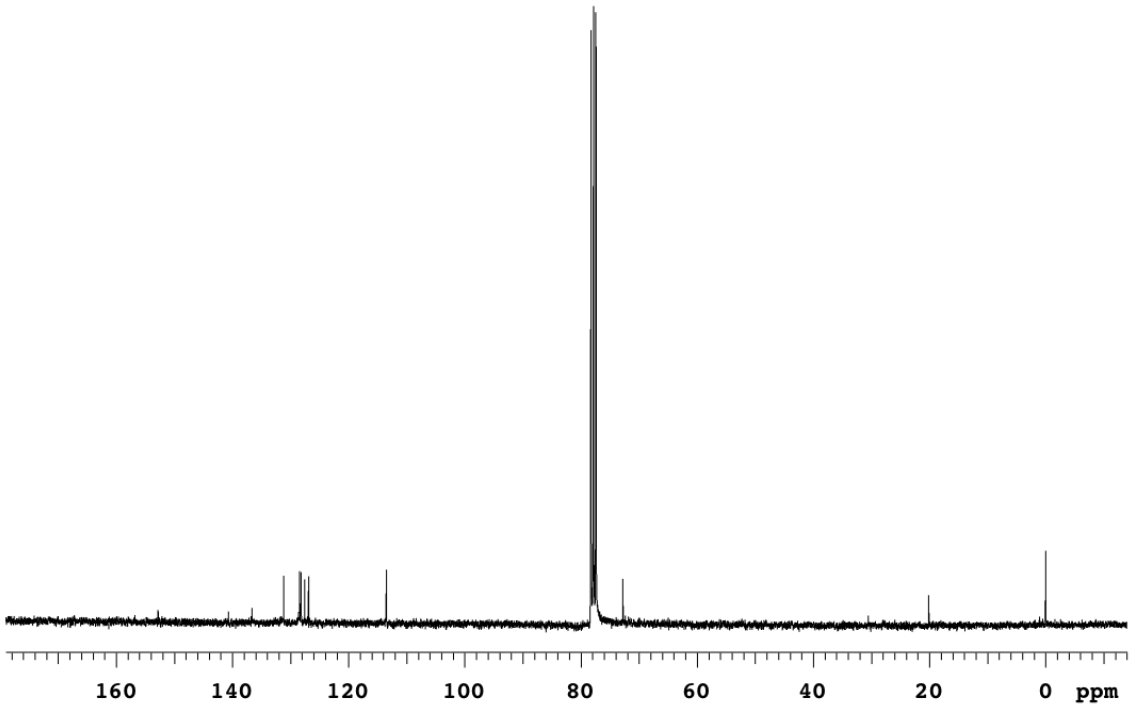
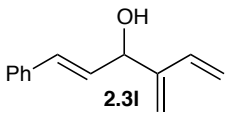


2.24

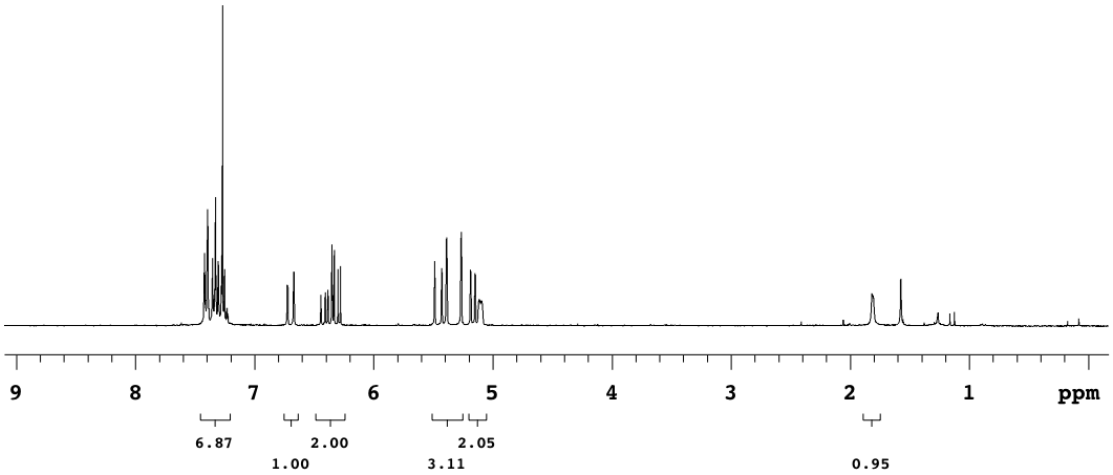
^{13}C NMR ($CDCl_3$, 75 MHz)



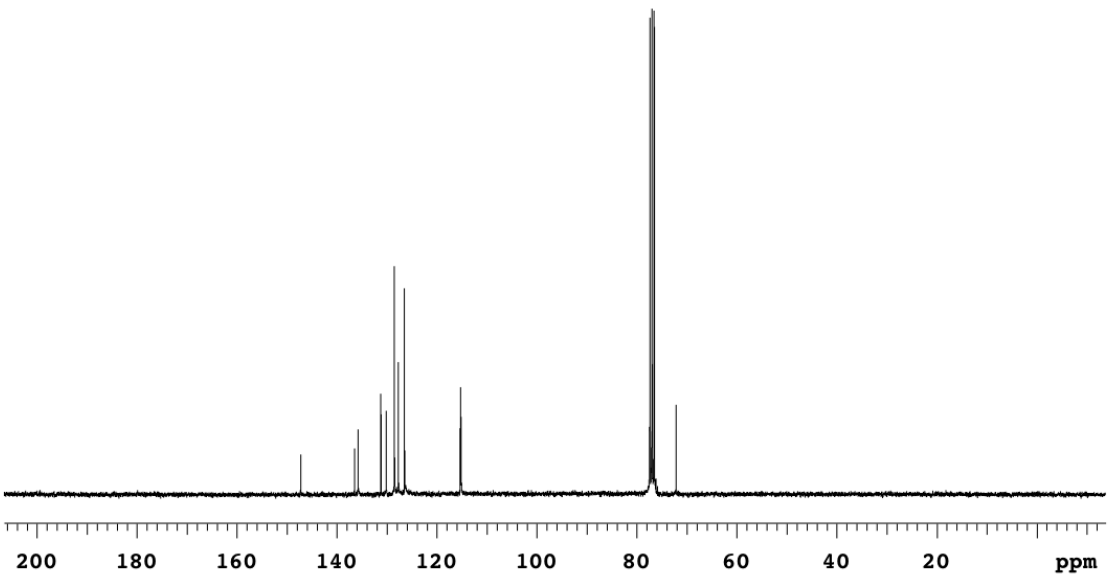
^{1}H NMR ($CDCl_3$, 300 MHz)



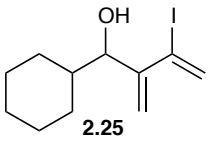
2.3l

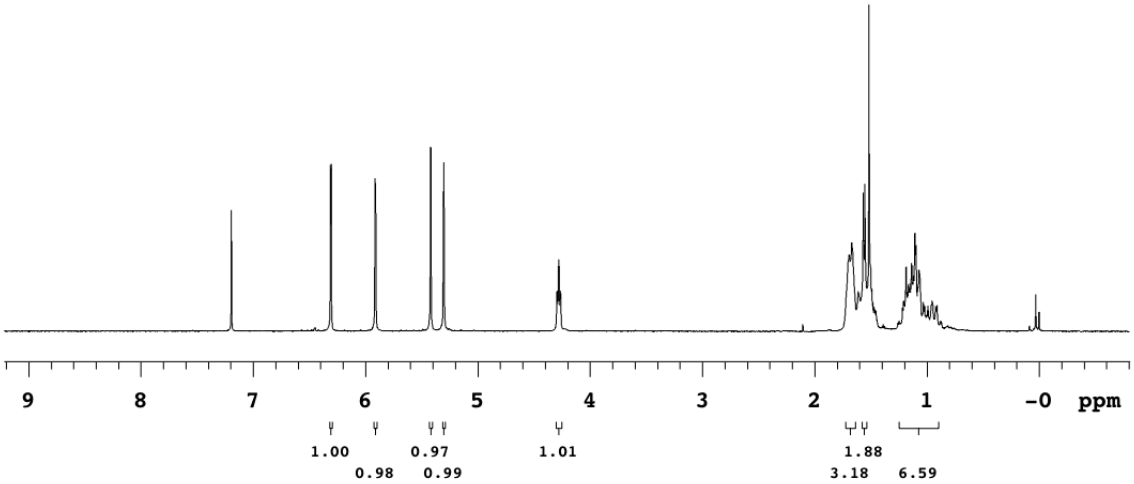


^{13}C NMR ($CDCl_3$, 75 MHz)

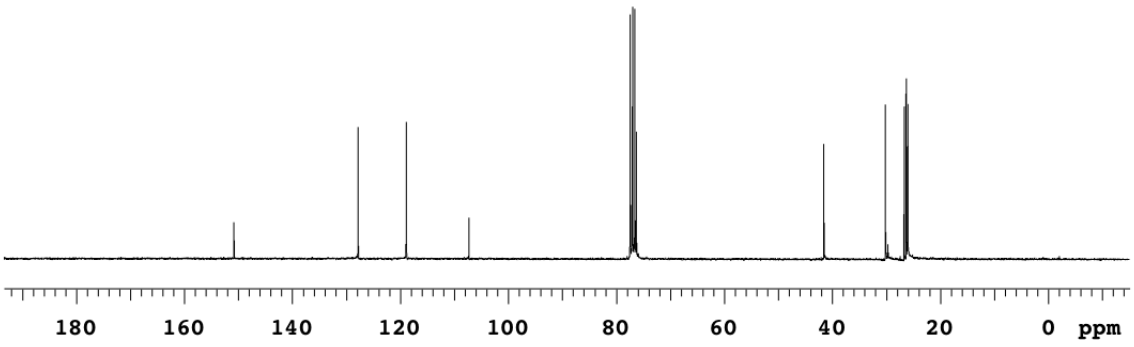


^{1}H NMR ($CDCl_3$, 300 MHz)

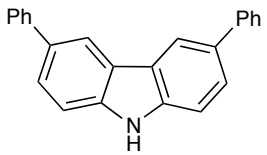




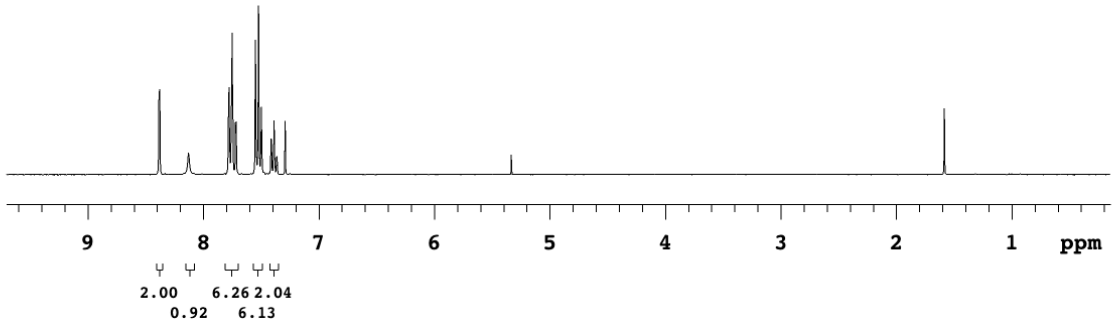
^{13}C NMR ($CDCl_3$, 75 MHz)



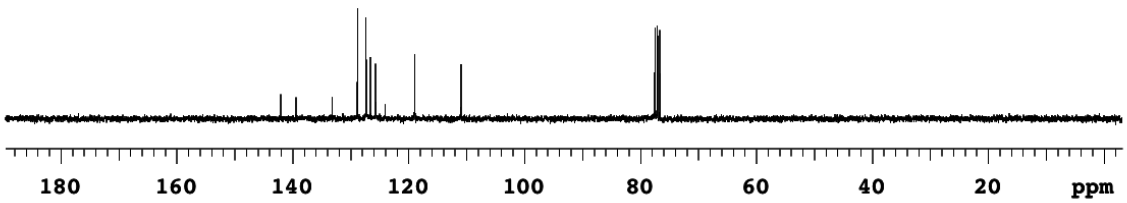
^{1}H NMR ($CDCl_3$, 300Hz)



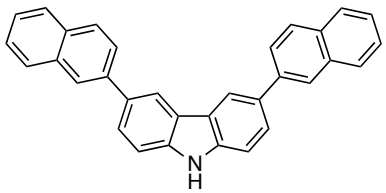
2.16a



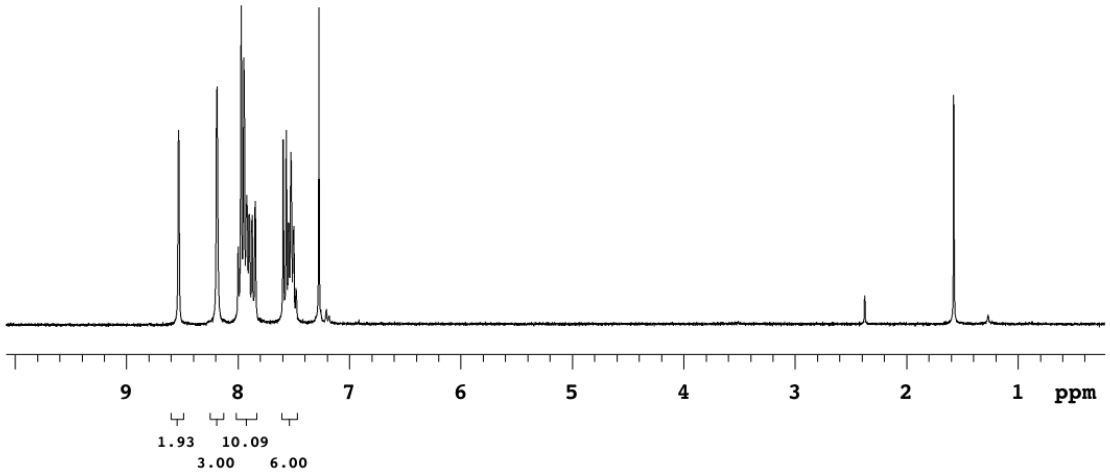
^{13}C NMR ($CDCl_3$, 75 MHz)



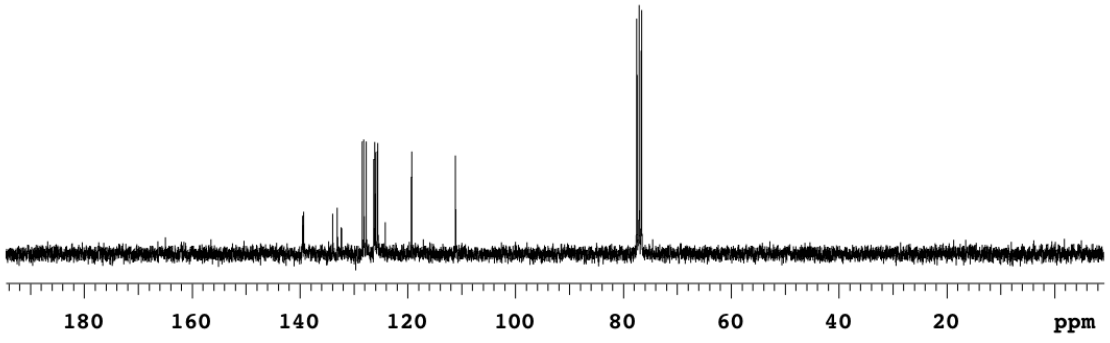
^{1}H NMR ($CDCl_3$, 300Hz)



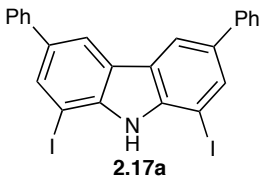
2.16c



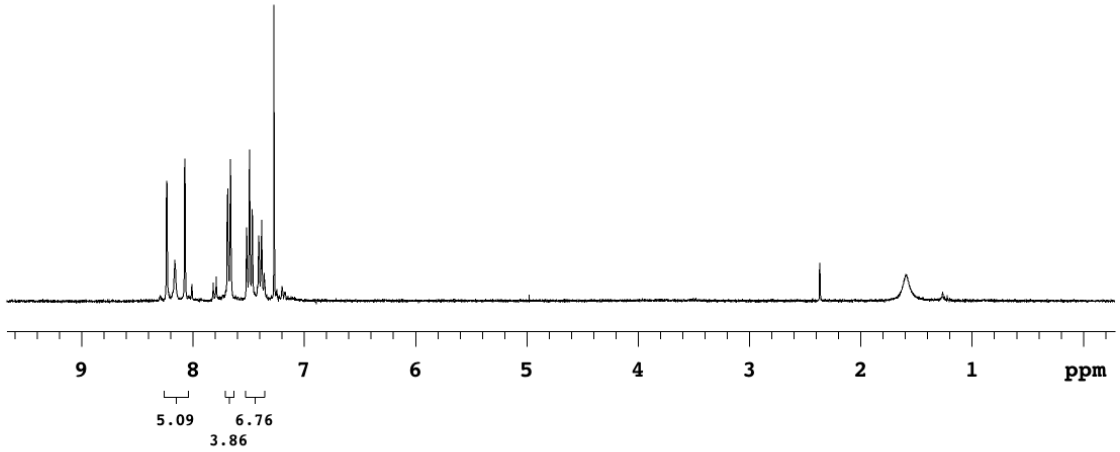
^{13}C NMR ($CDCl_3$, 75 MHz)



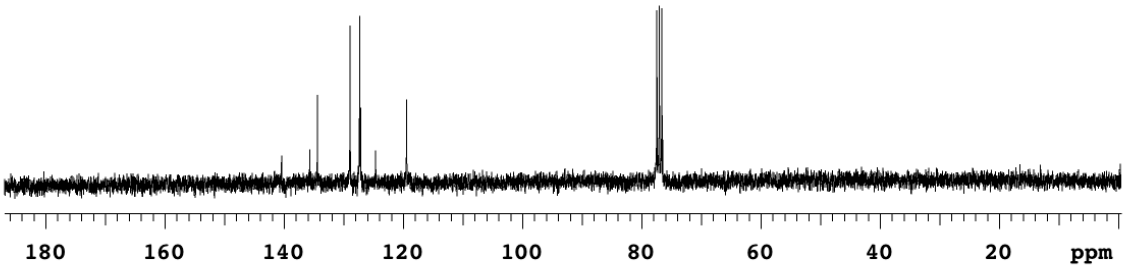
^{1}H NMR ($CDCl_3$, 300Hz)



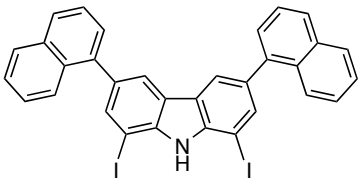
2.17a



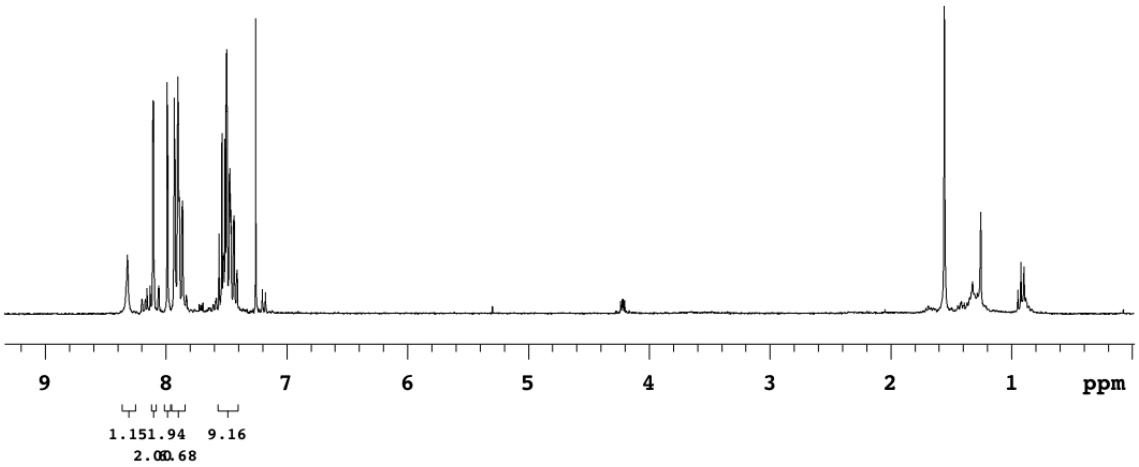
^{13}C NMR ($CDCl_3$, 300 MHz)



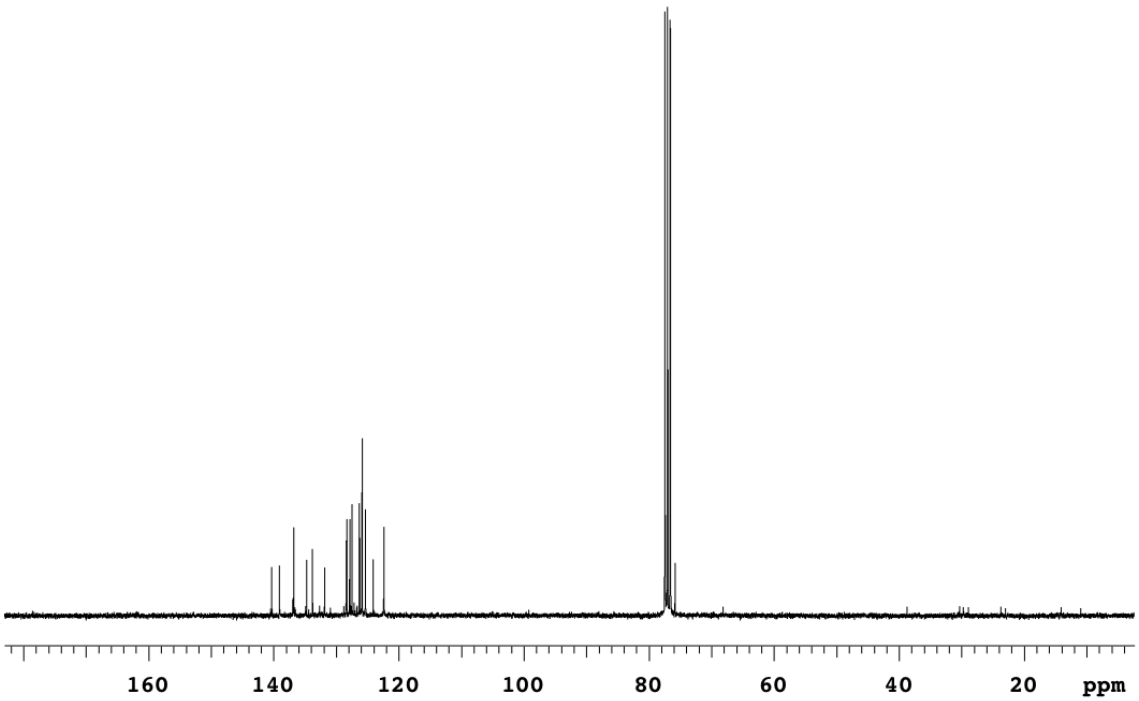
^{1}H NMR ($CDCl_3$, 300Hz)



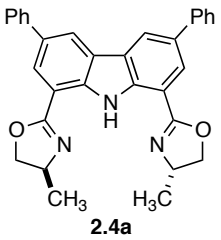
2.17b



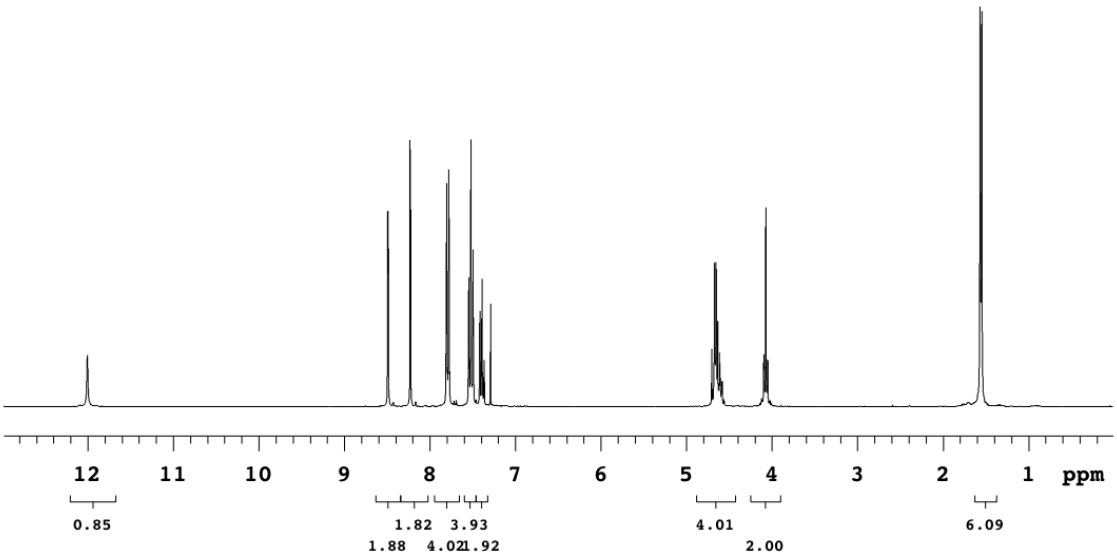
^{13}C NMR ($CDCl_3$, 300 MHz)



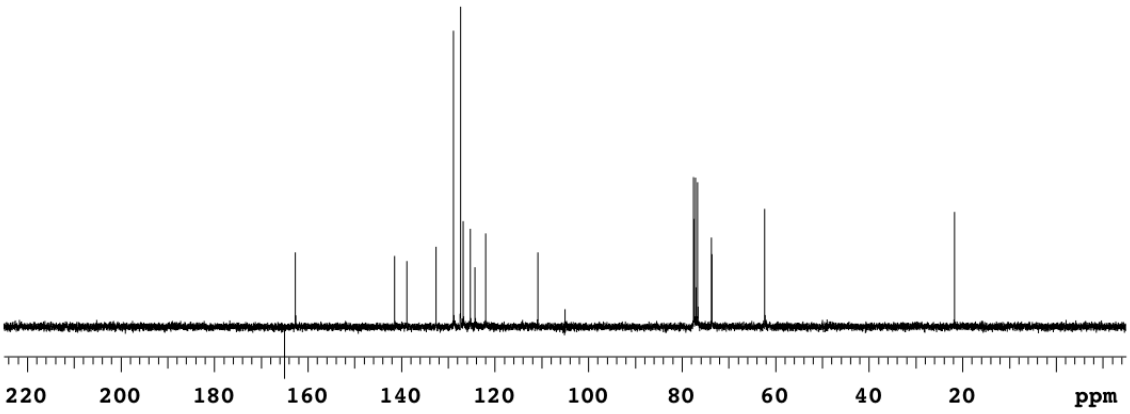
^{1}H NMR ($CDCl_3$, 75 MHz)



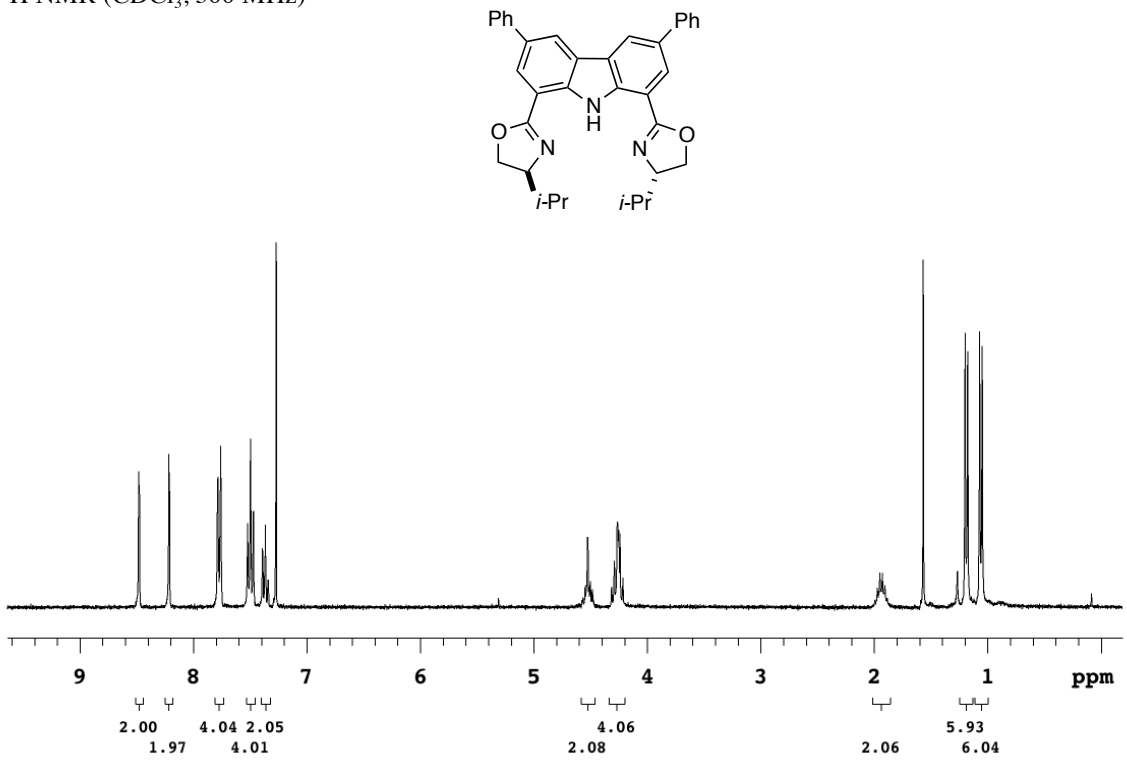
2.4a



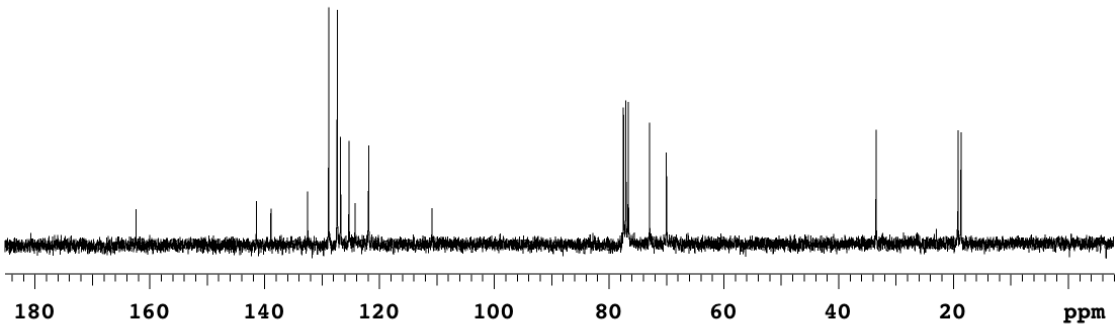
^{13}C NMR ($CDCl_3$, 300 MHz)



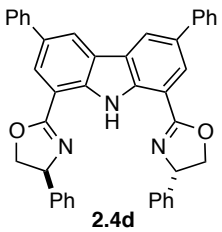
^{1}H NMR ($CDCl_3$, 300 MHz)



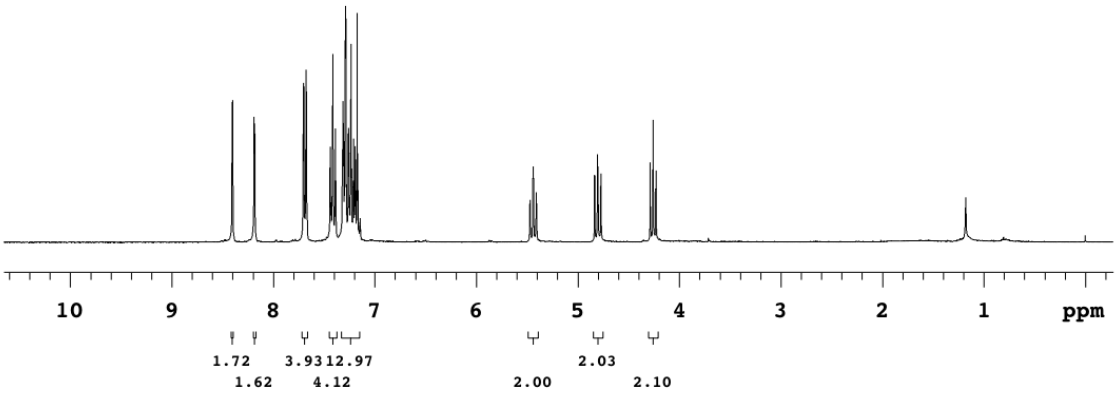
^{13}C NMR ($CDCl_3$, 75 MHz)



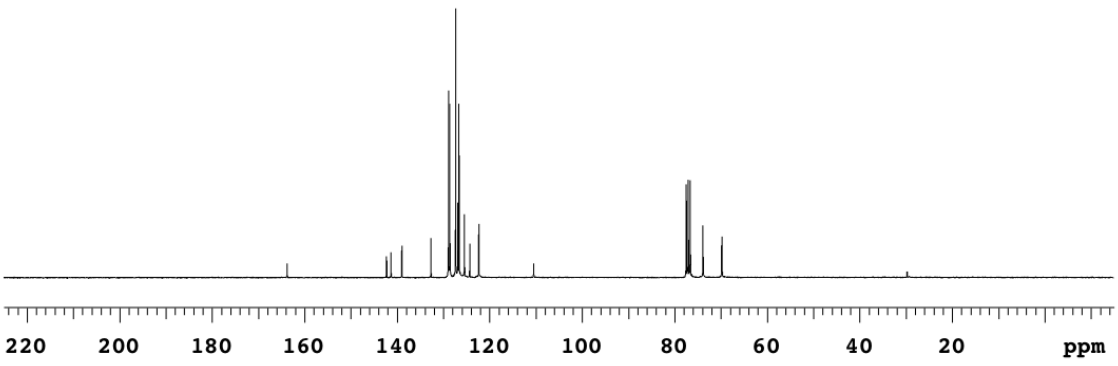
^{1}H NMR ($CDCl_3$, 300 MHz)



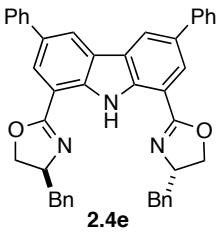
2.4d



^{13}C NMR ($CDCl_3$, 75 MHz)

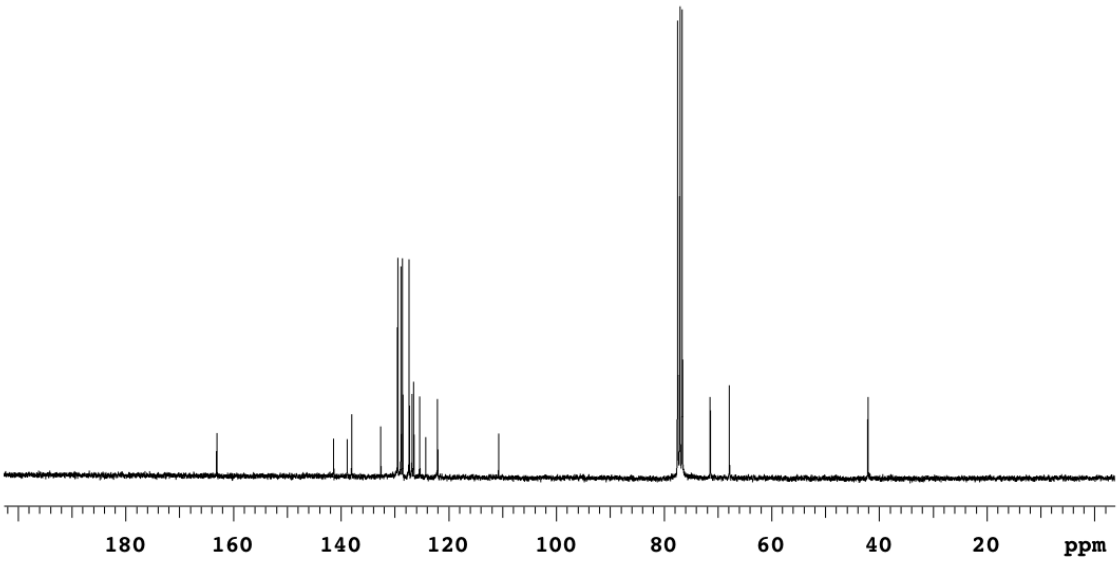


^{1}H NMR ($CDCl_3$, 300 MHz)

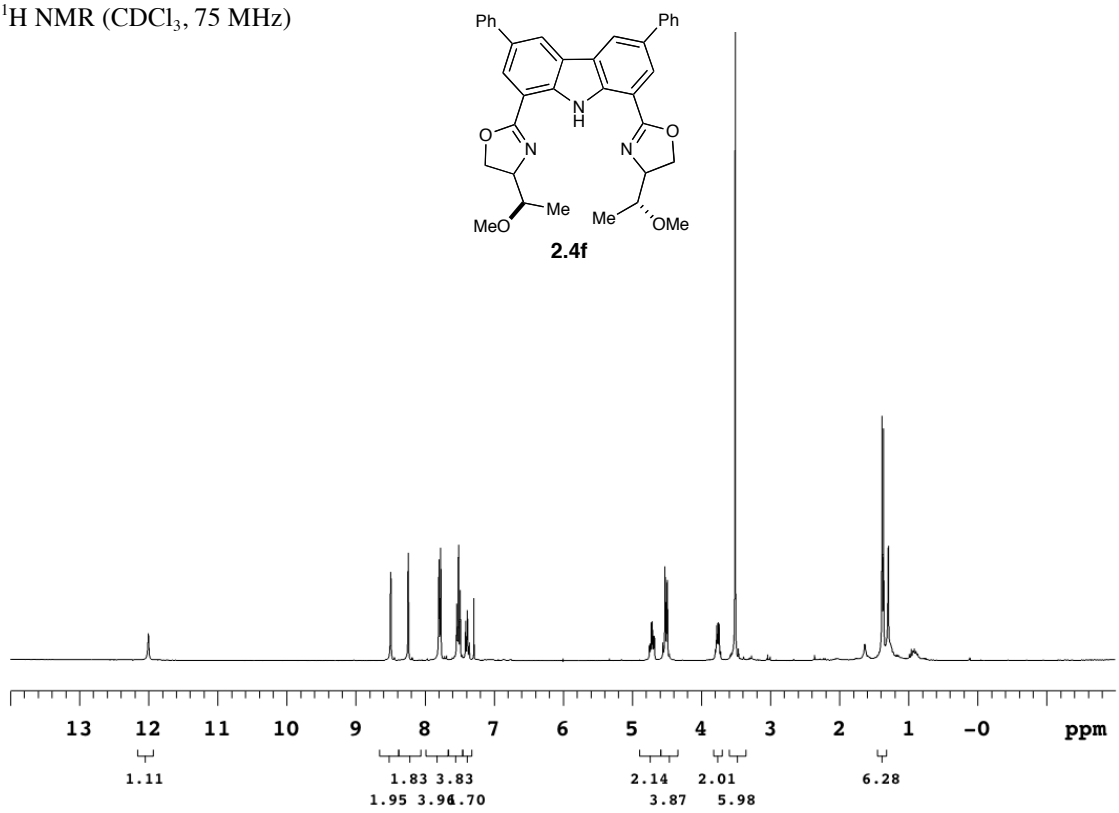


2.4e

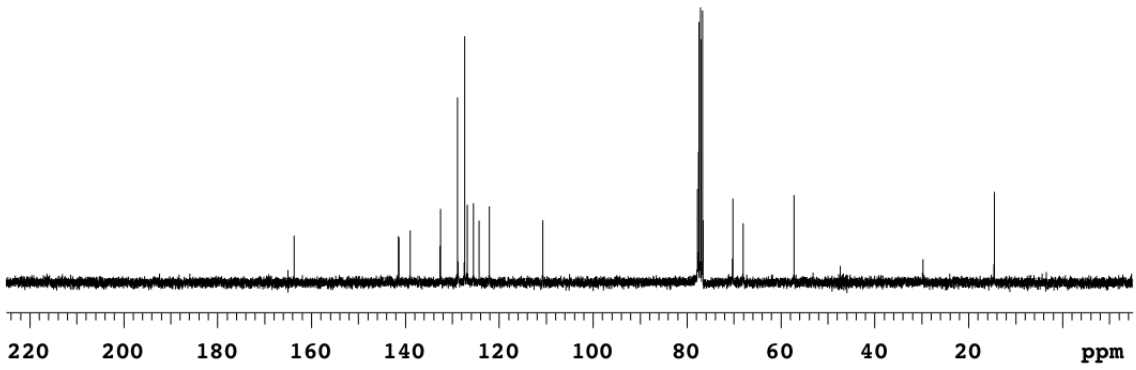
^{13}C NMR ($CDCl_3$, 75 MHz)



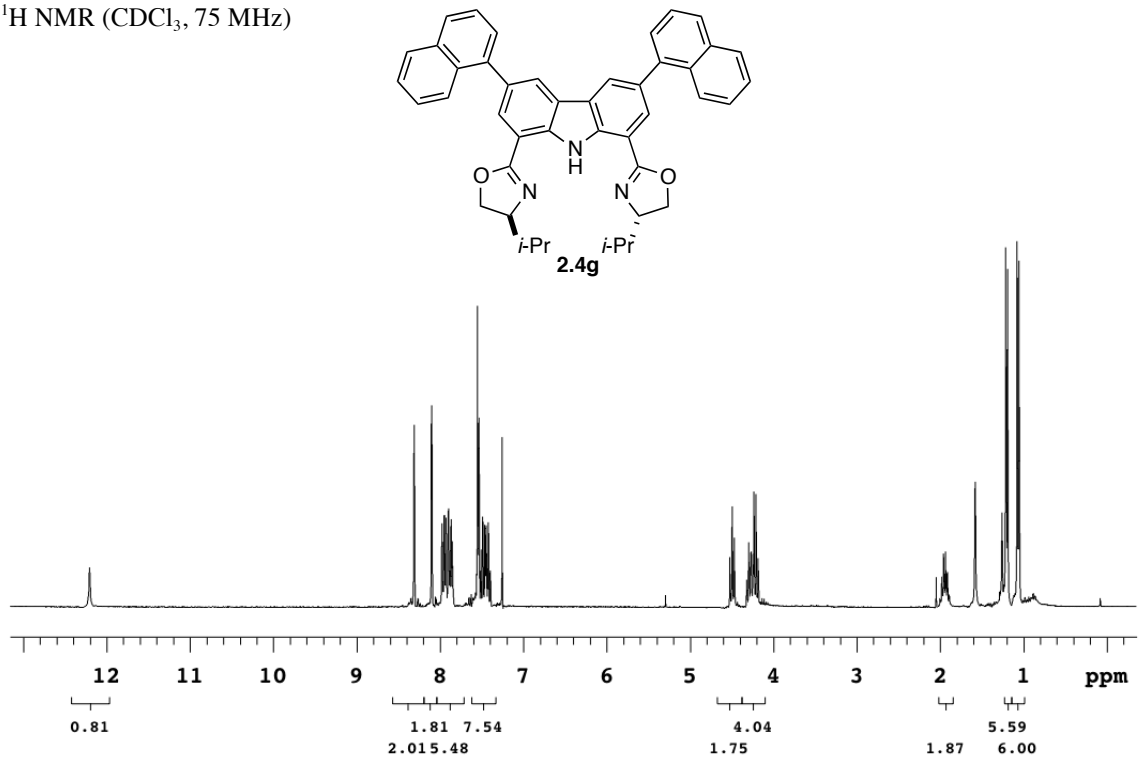
^{1}H NMR ($CDCl_3$, 75 MHz)



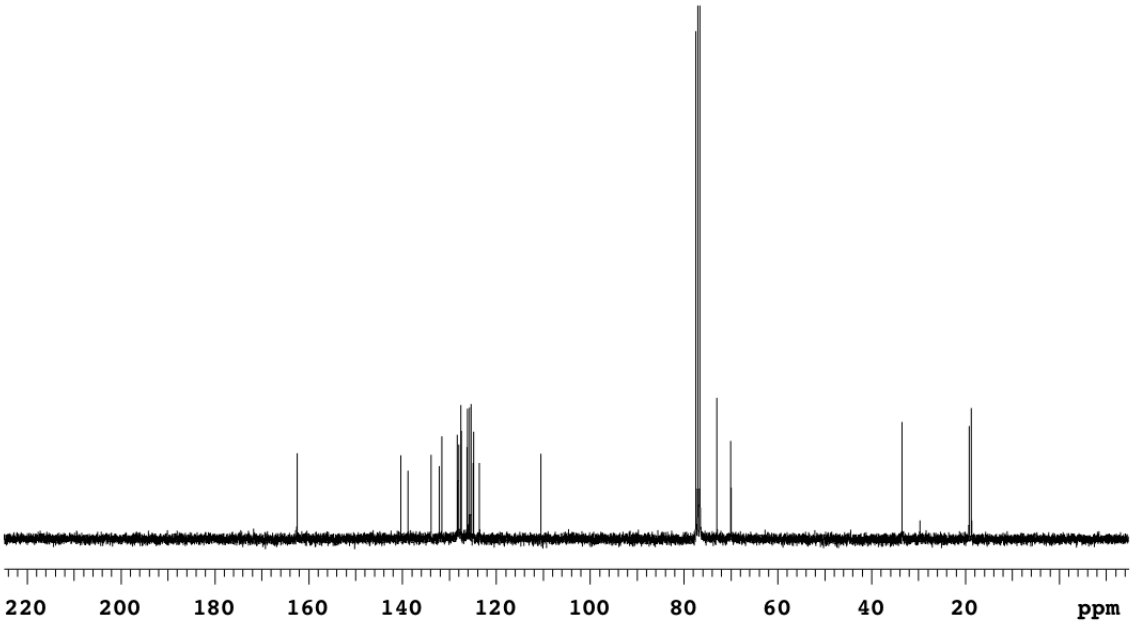
^{13}C NMR ($CDCl_3$, 300 MHz)



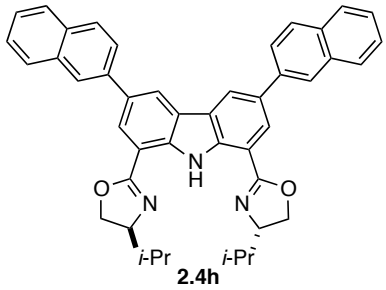
^{1}H NMR ($CDCl_3$, 75 MHz)



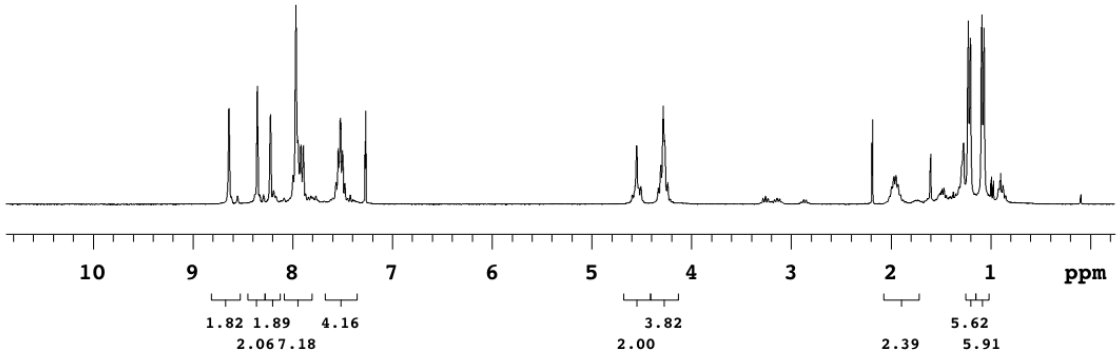
^{13}C NMR ($CDCl_3$, 300 MHz)



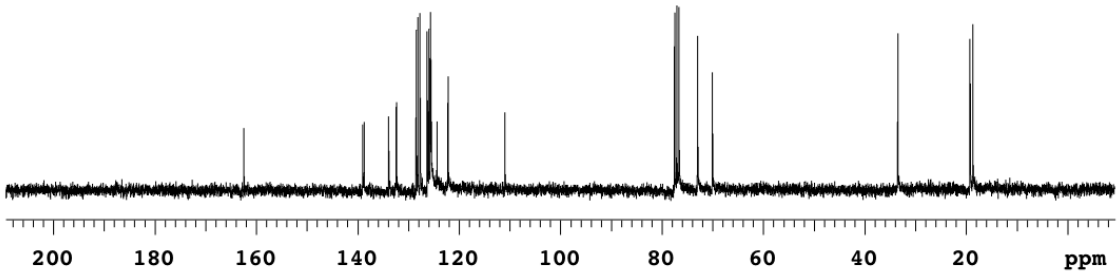
^{1}H NMR ($CDCl_3$, 300Hz)



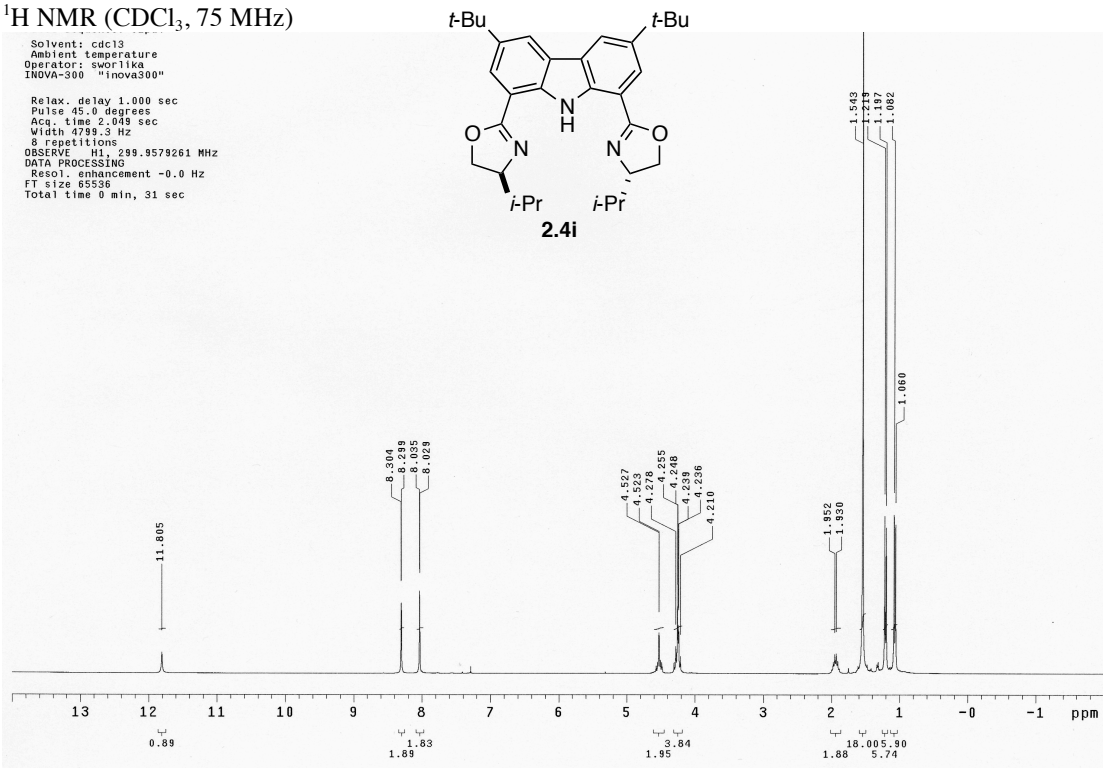
2.4h



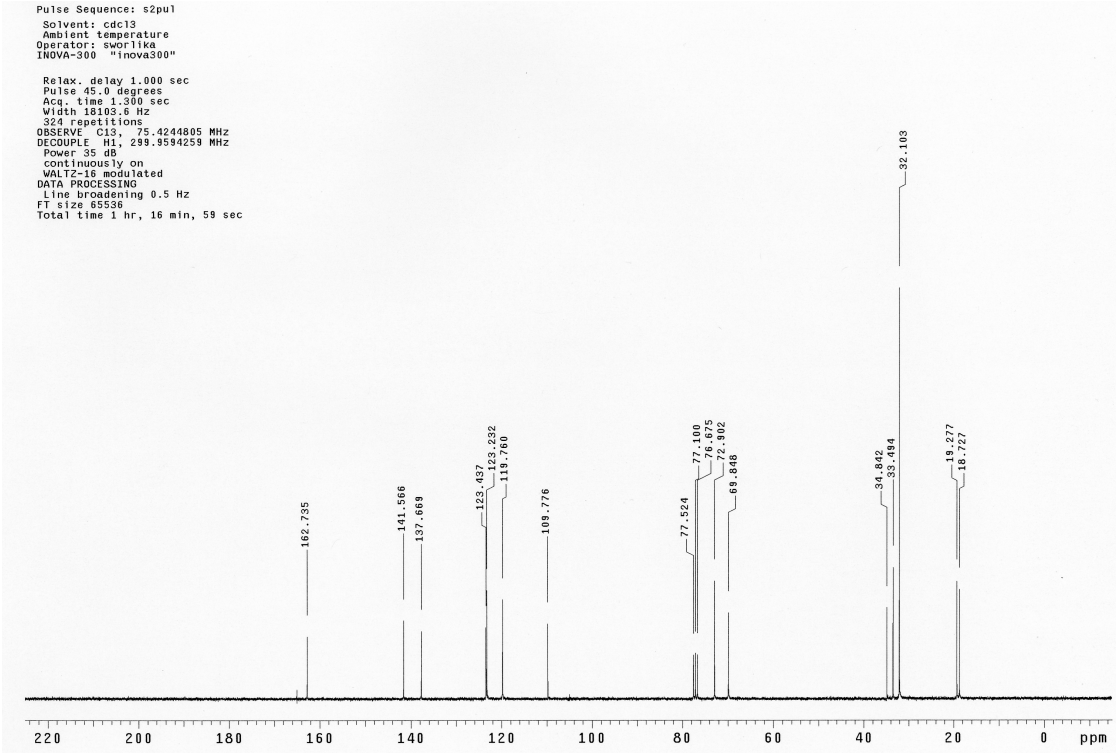
^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 75 MHz)

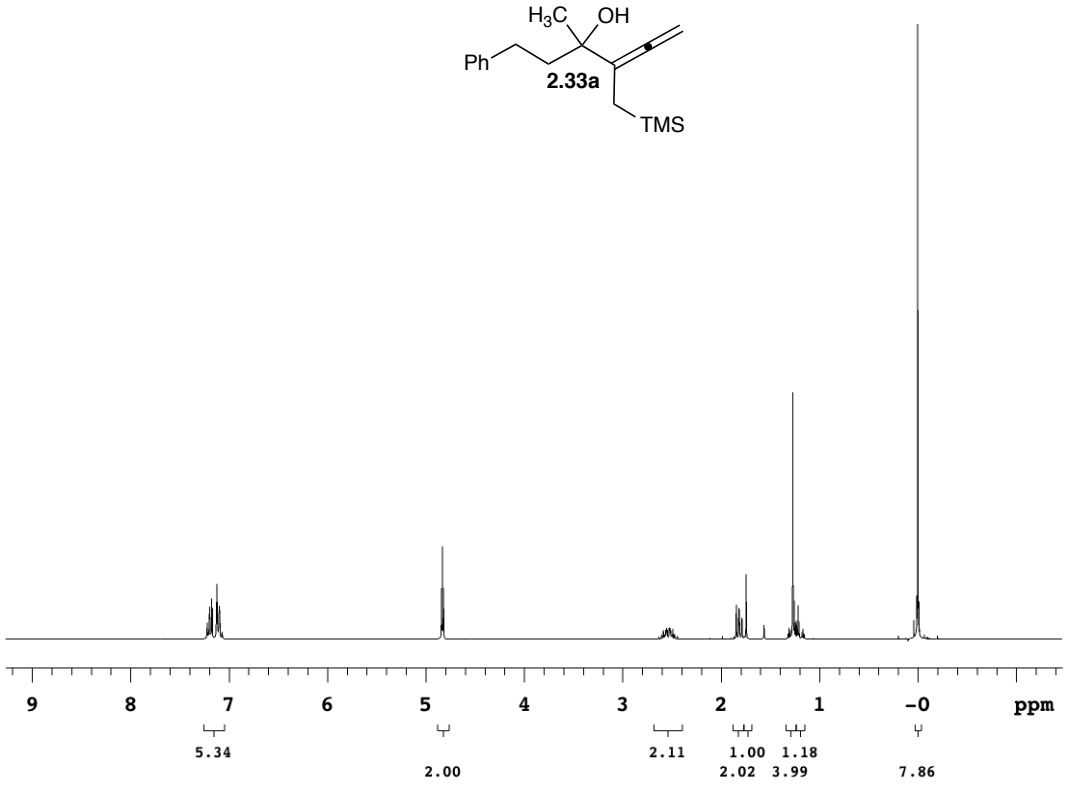


^{13}C NMR ($CDCl_3$, 300 MHz)

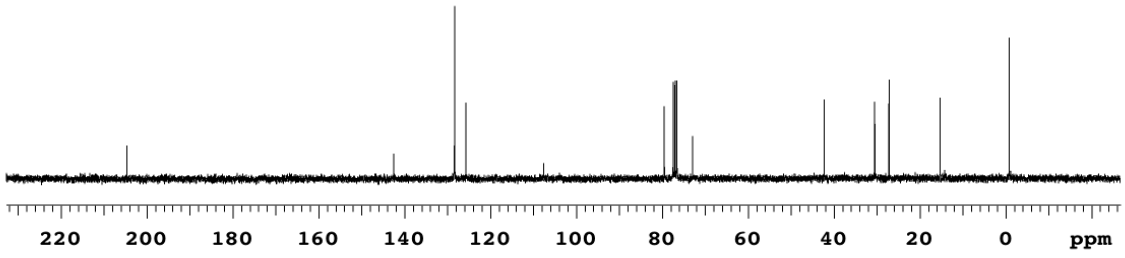


KETONES

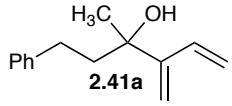
^{1}H NMR ($CDCl_3$, 300 MHz)



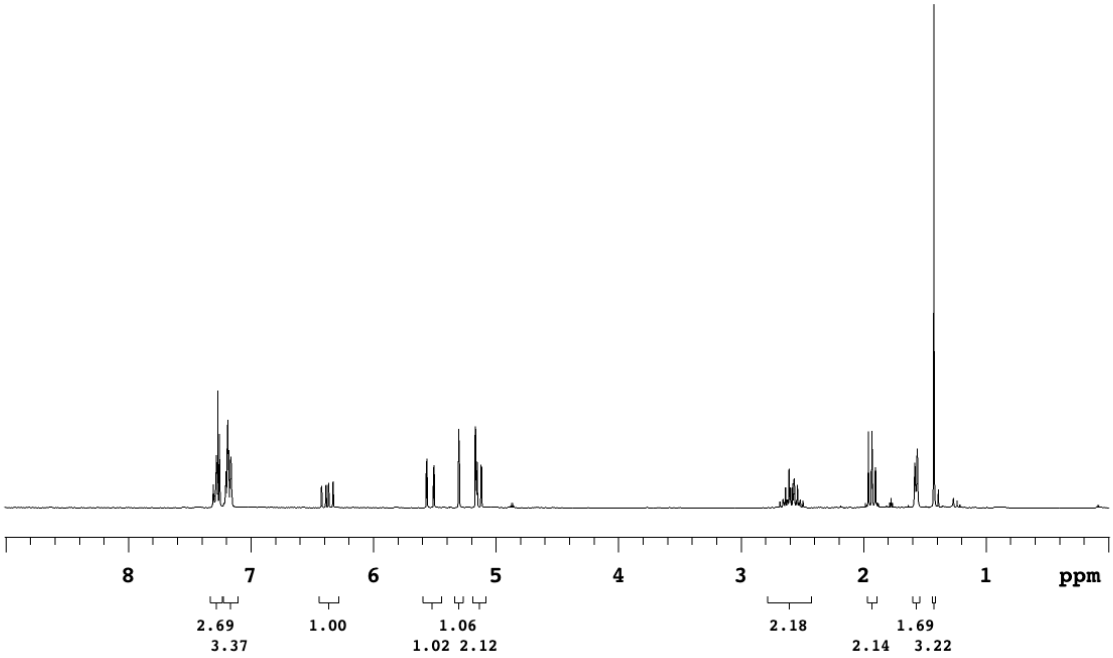
^{13}C NMR ($CDCl_3$, 75 MHz)



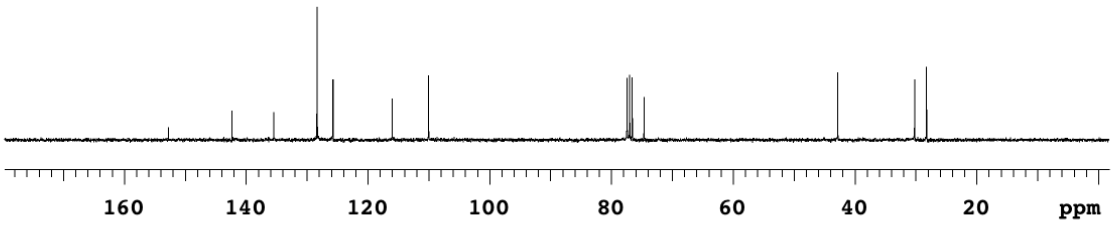
^{1}H NMR ($CDCl_3$, 300 MHz)



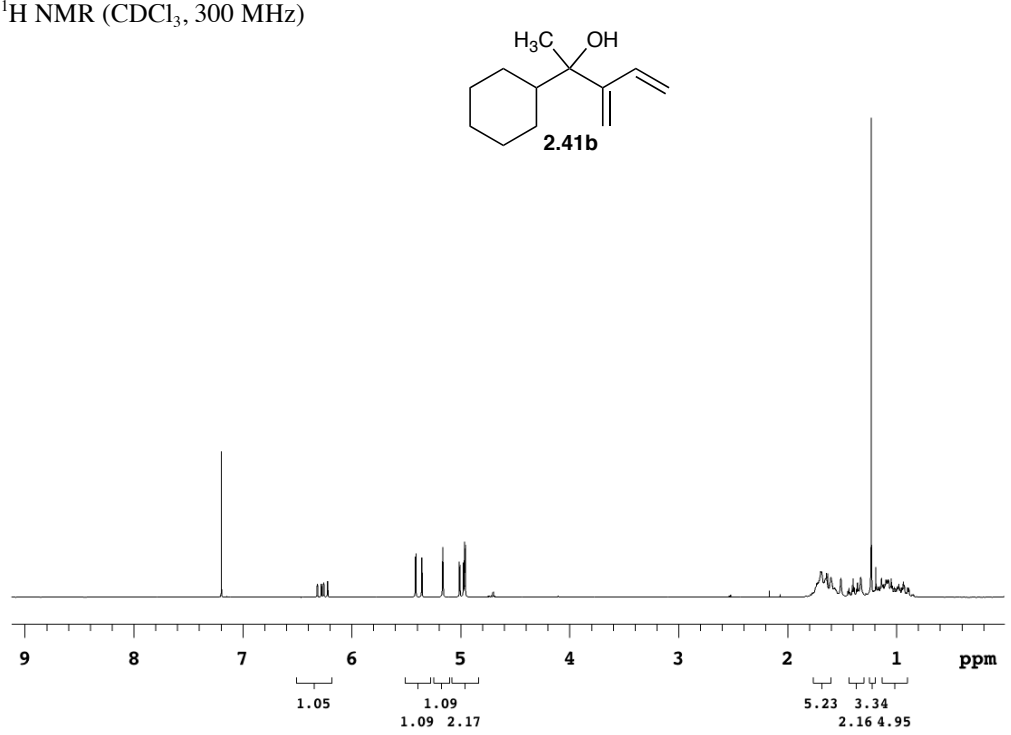
2.41a



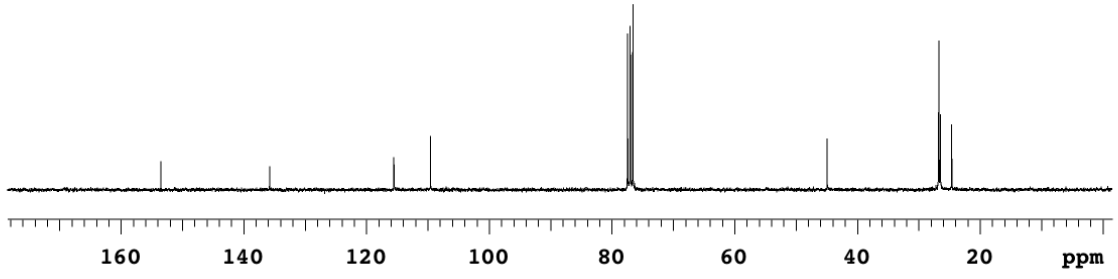
^{13}C NMR ($CDCl_3$, 75 MHz)



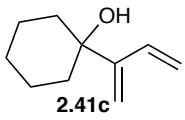
^{1}H NMR ($CDCl_3$, 300 MHz)



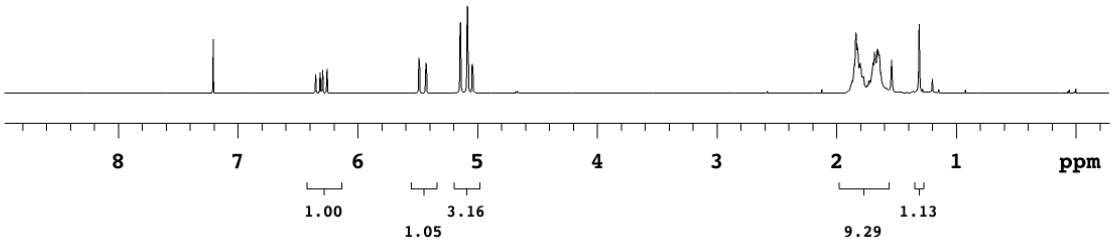
^{13}C NMR ($CDCl_3$, 75 MHz)



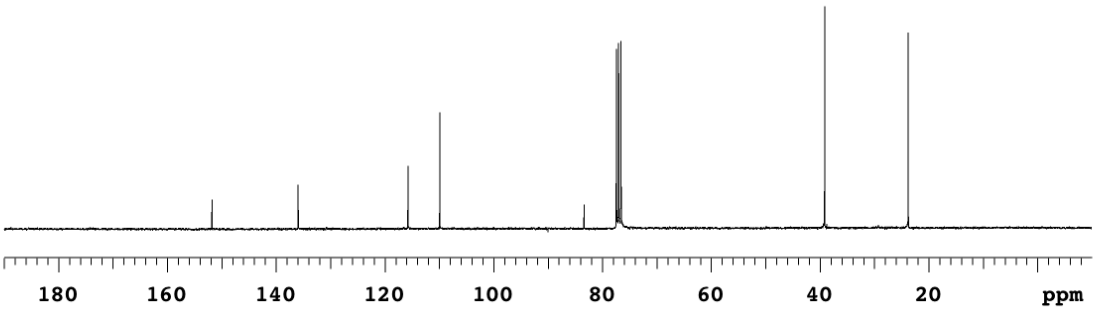
^{1}H NMR ($CDCl_3$, 300 MHz)



2.41c



^{13}C NMR ($CDCl_3$, 75 MHz)



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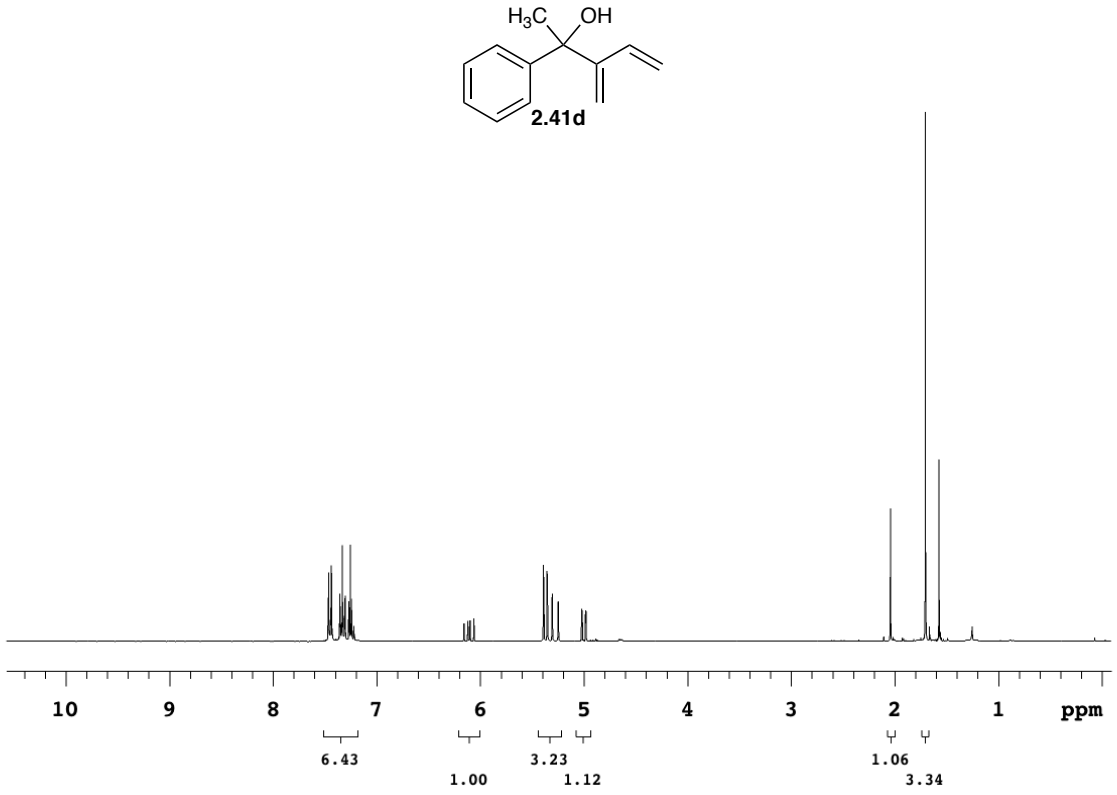

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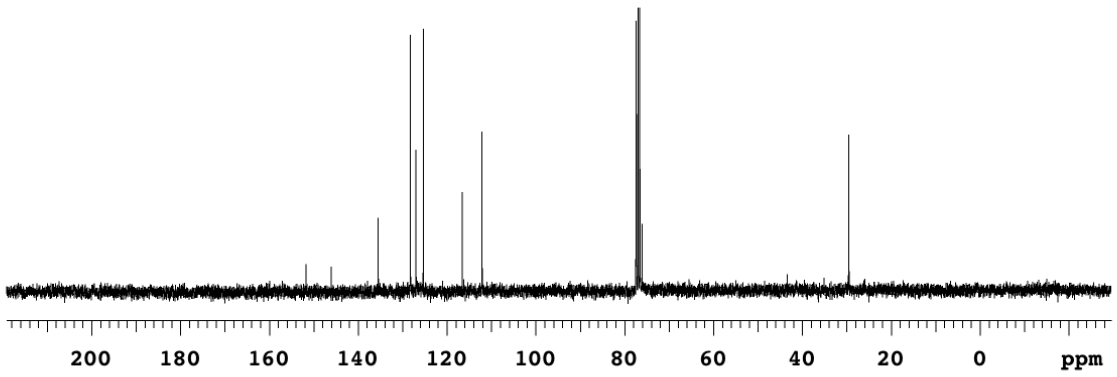
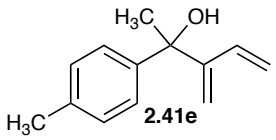
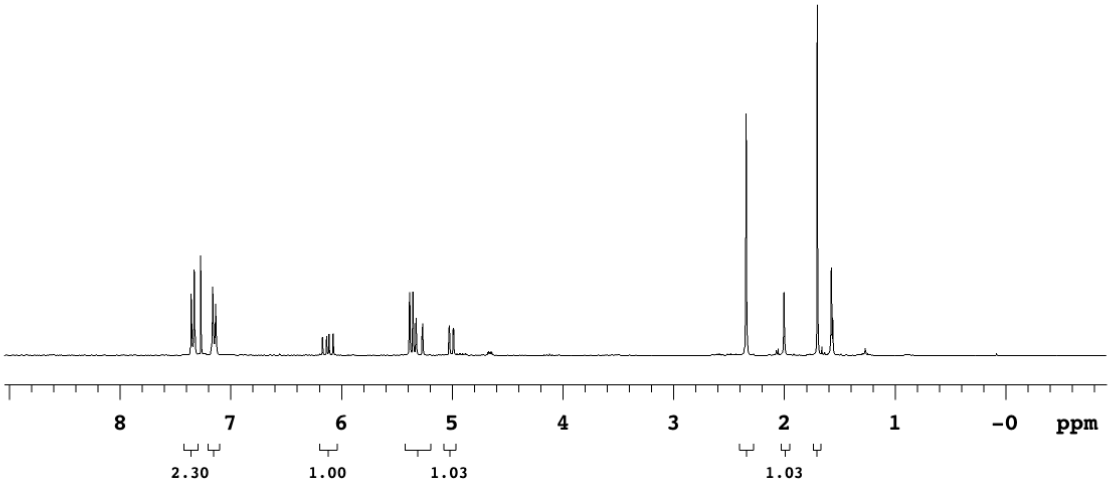
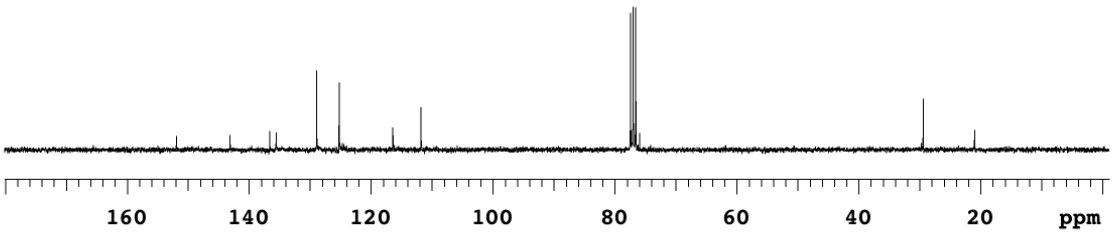


^{1}H NMR ($CDCl_3$, 300 MHz)

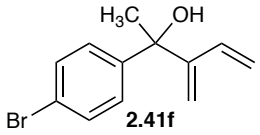




^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



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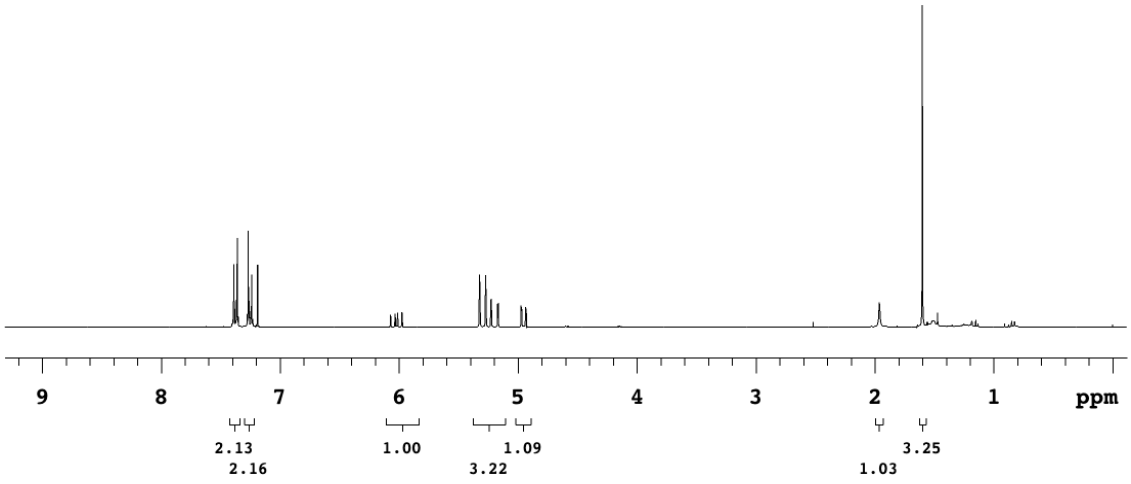

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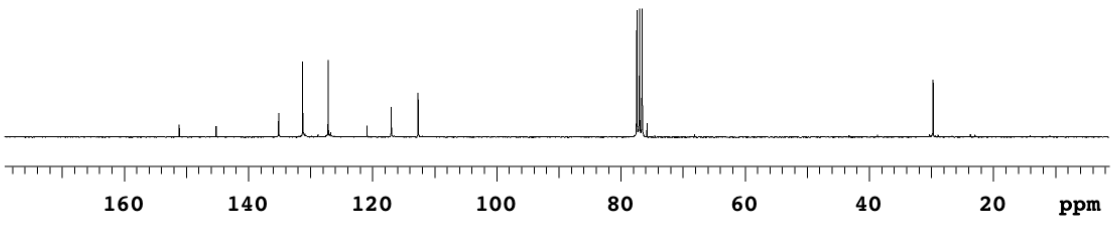

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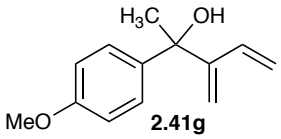

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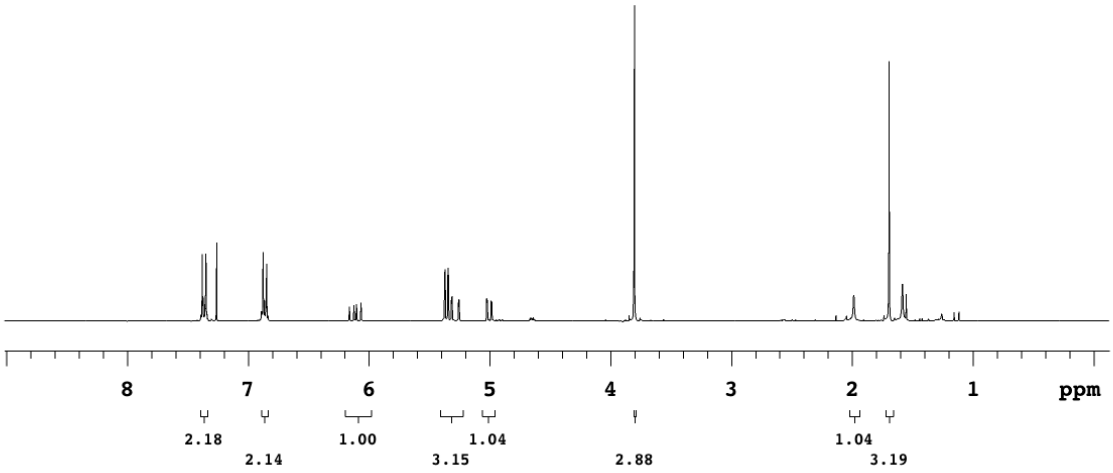

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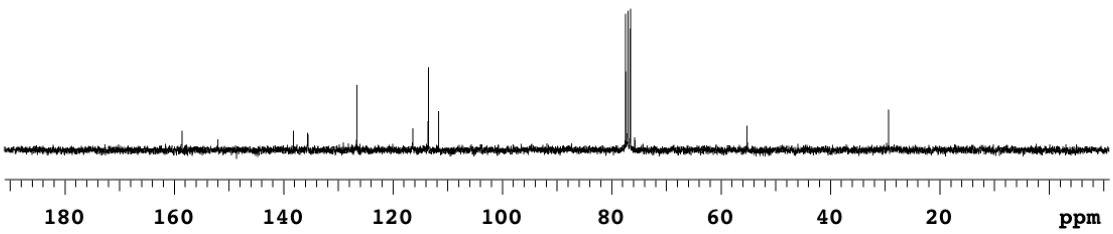

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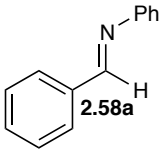
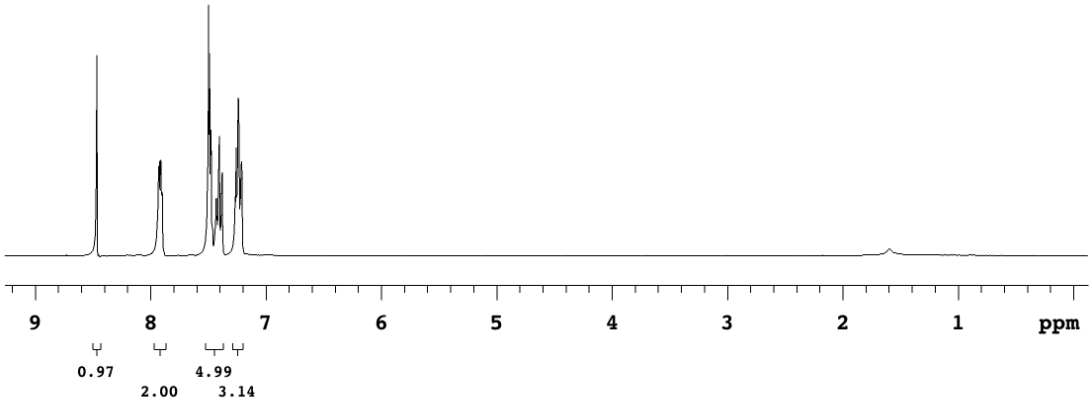
^{1}H NMR ($CDCl_3$, 300 MHz)





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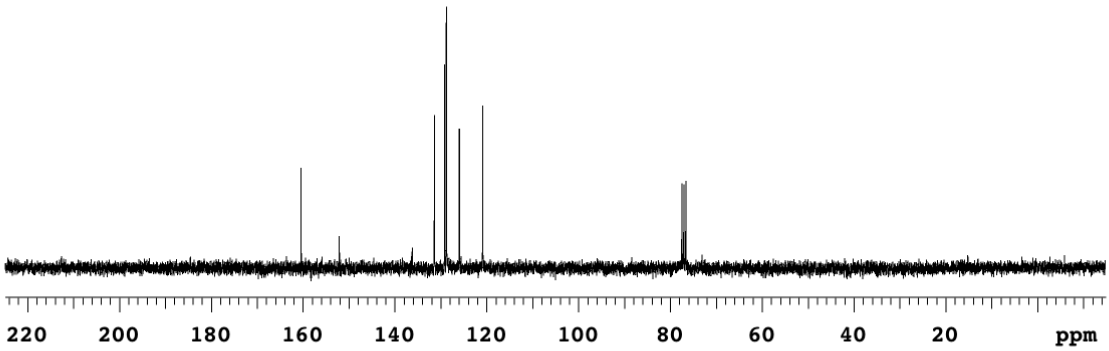

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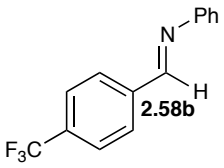

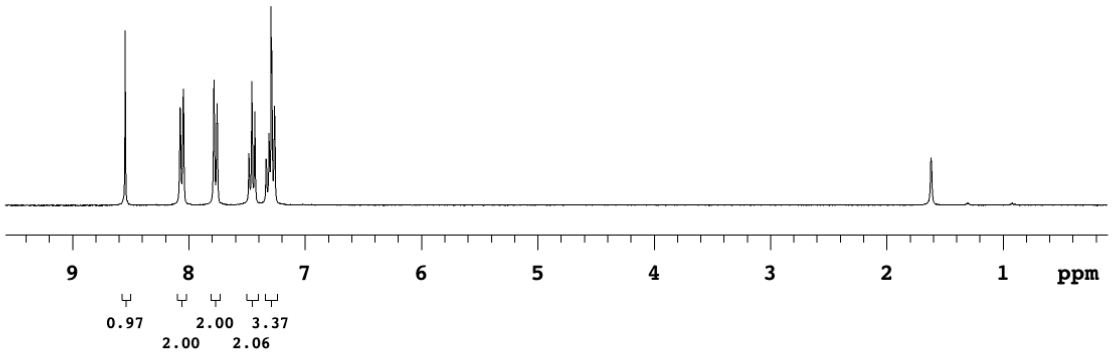

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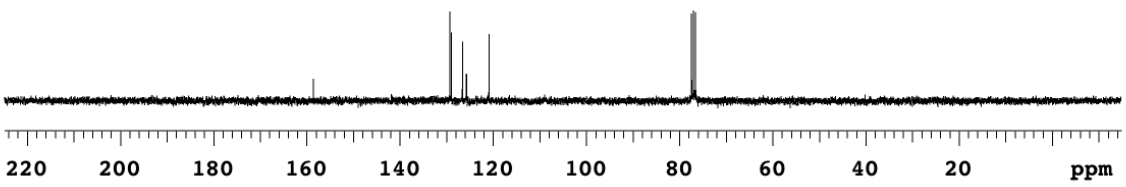

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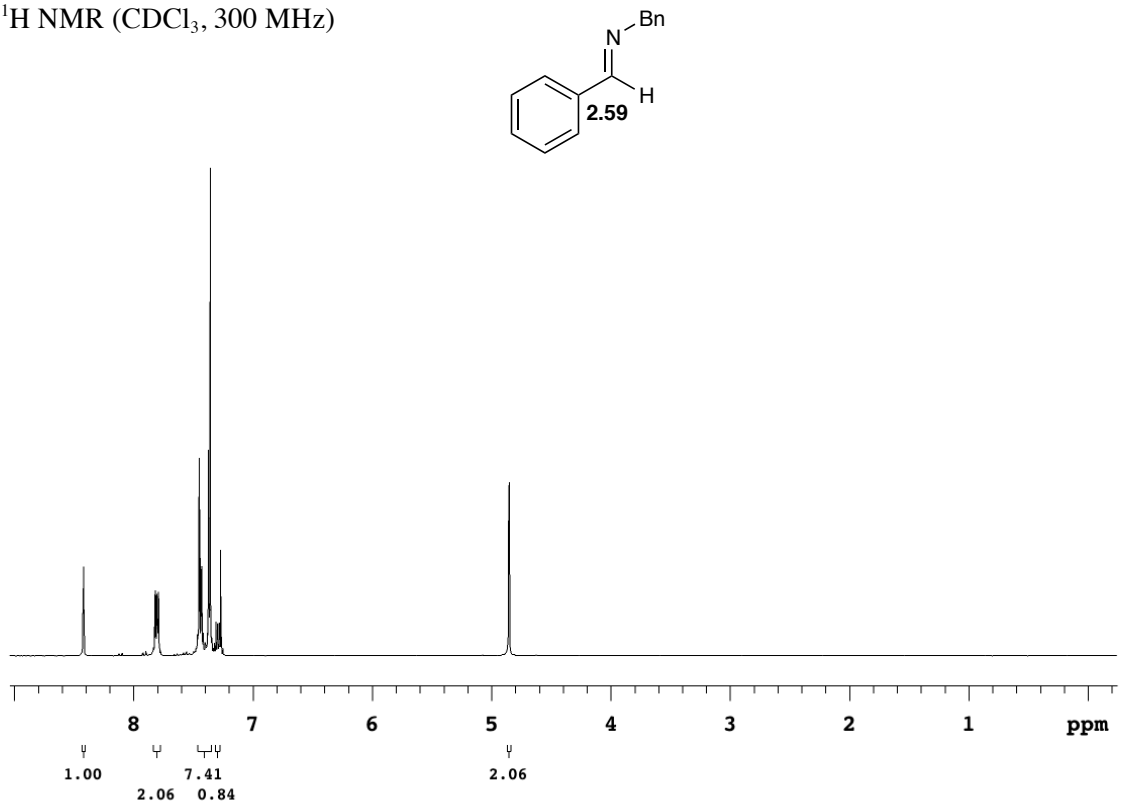

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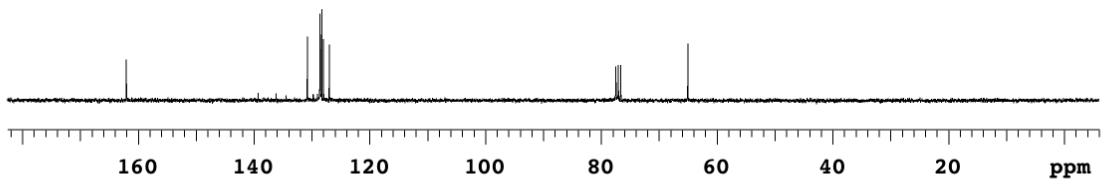

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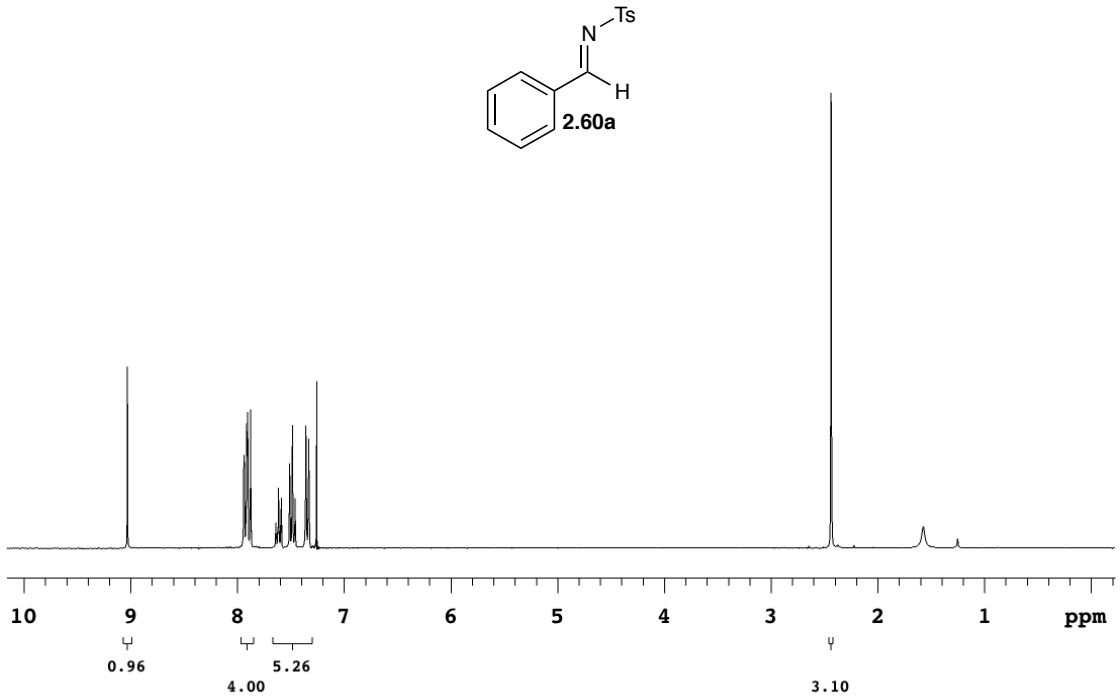

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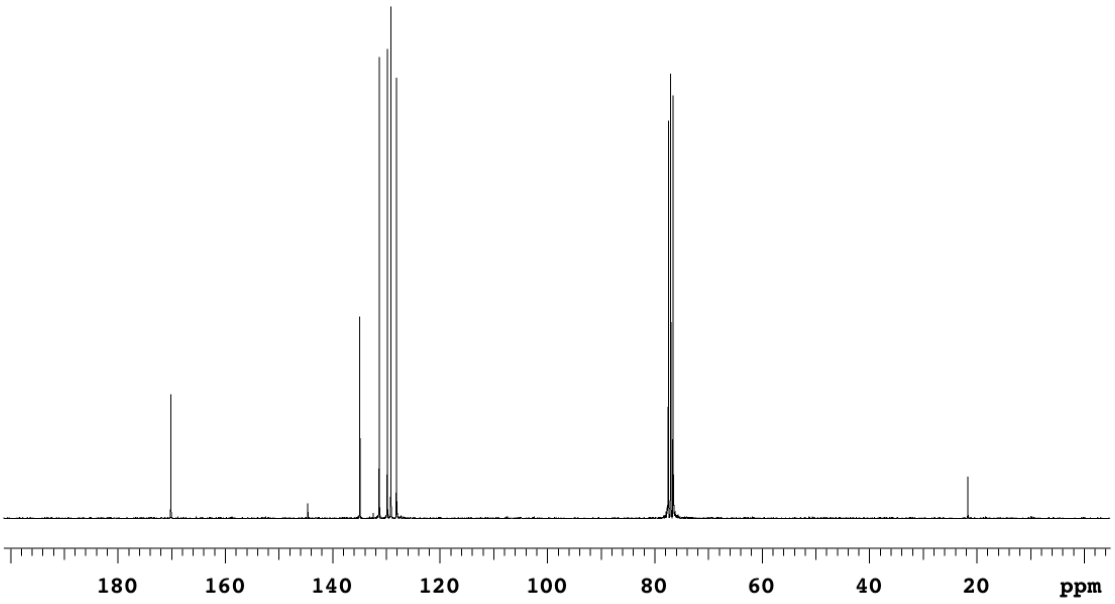

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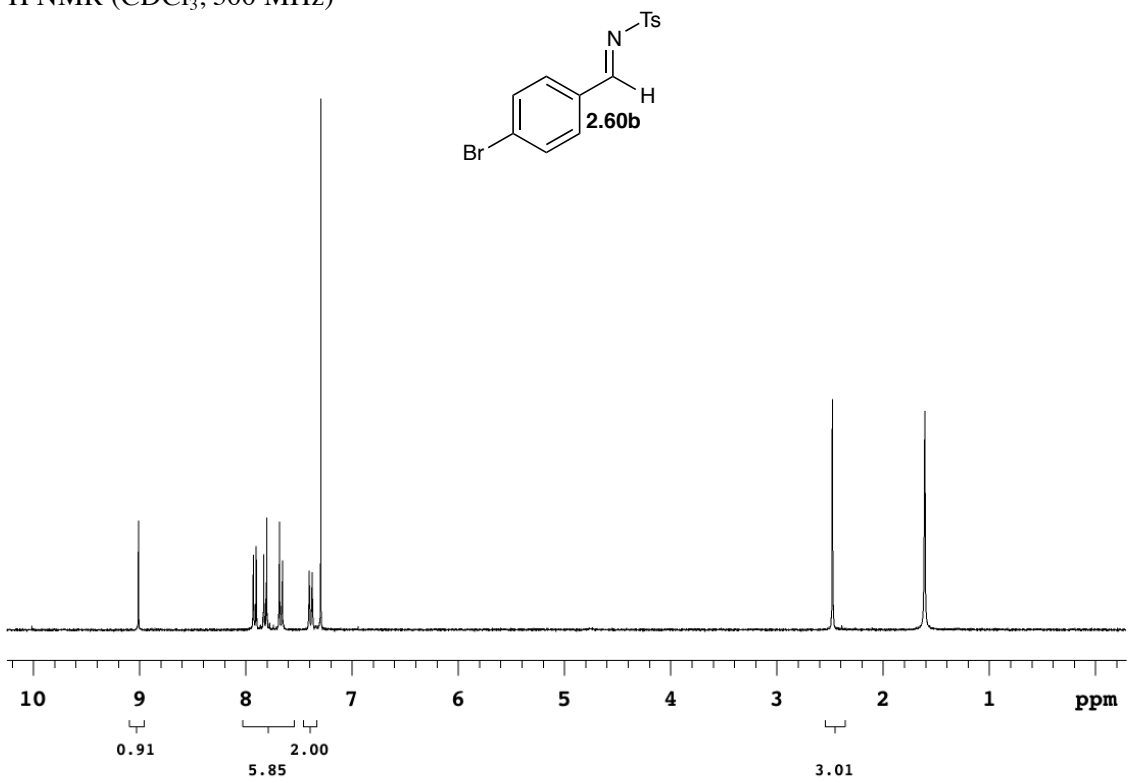

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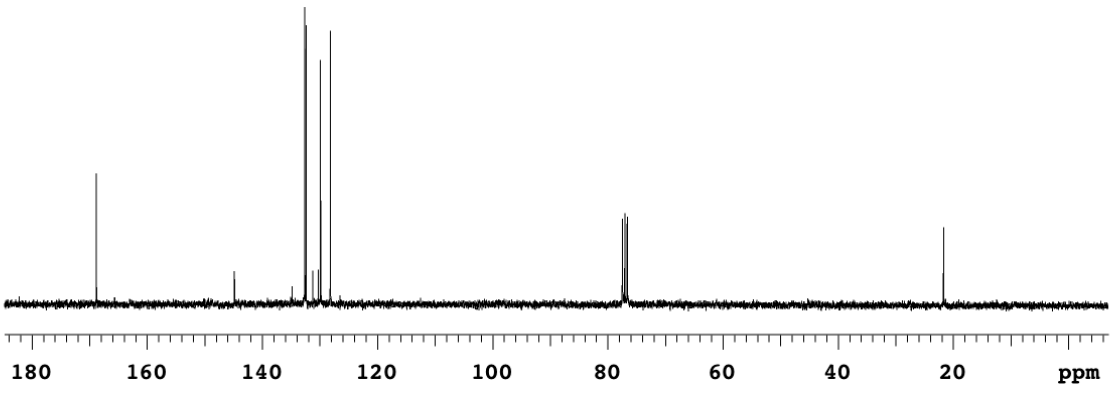

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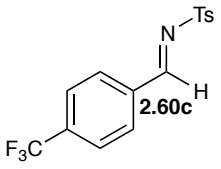

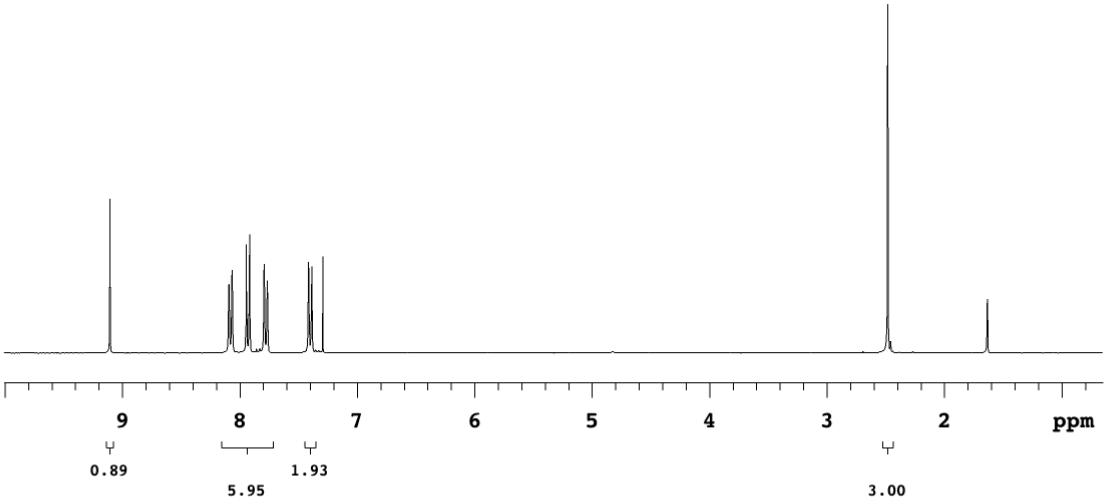

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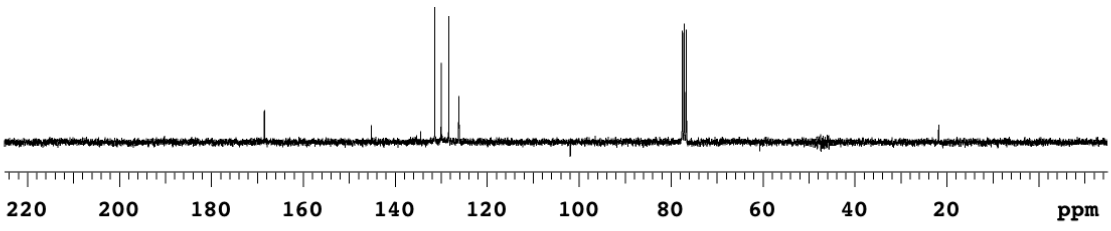

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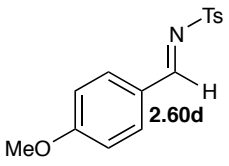

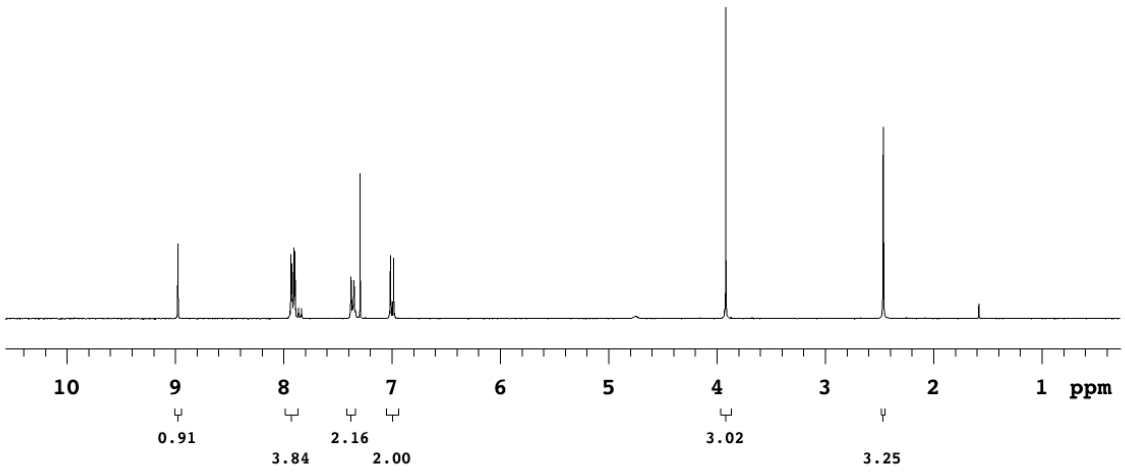

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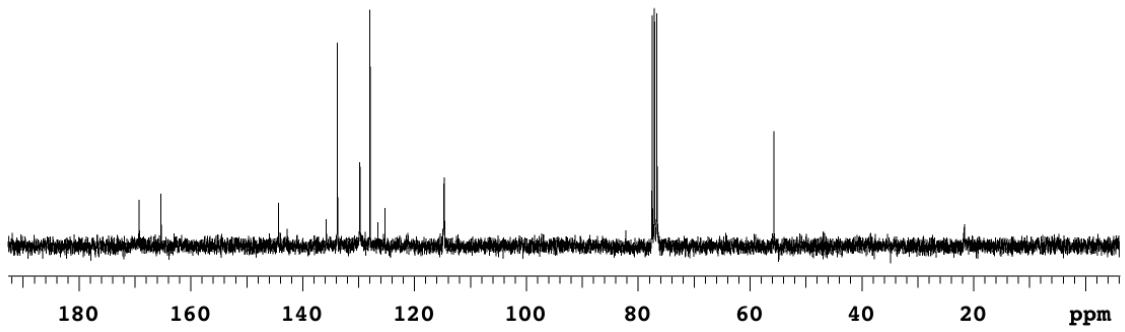

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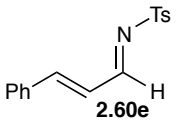

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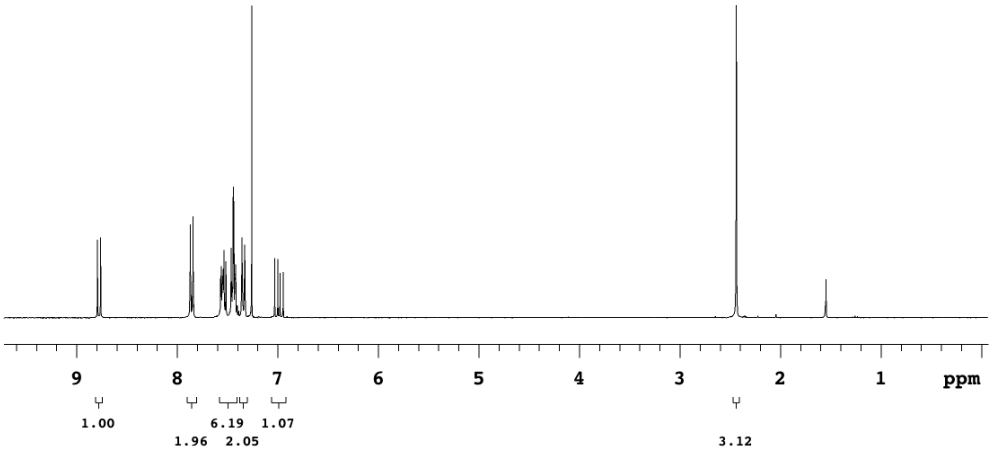

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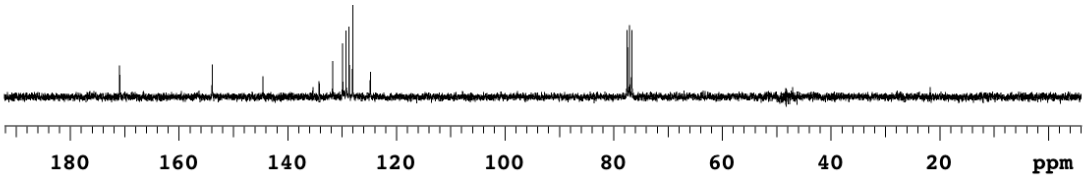

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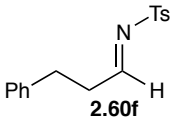

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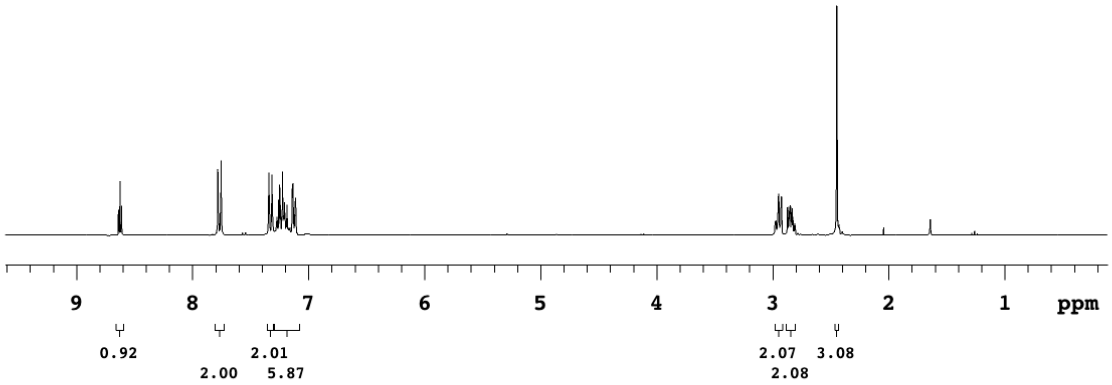

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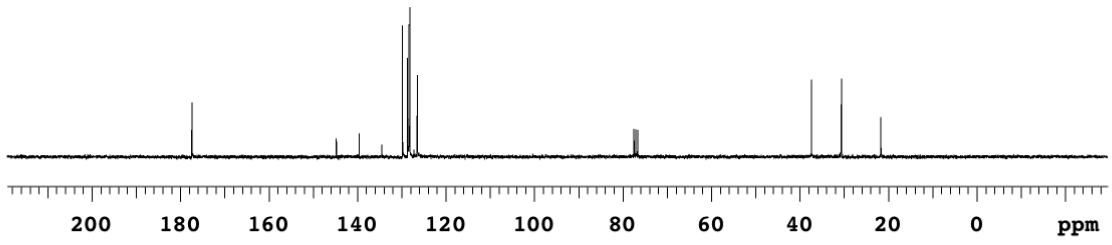

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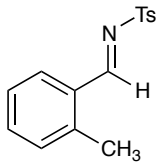

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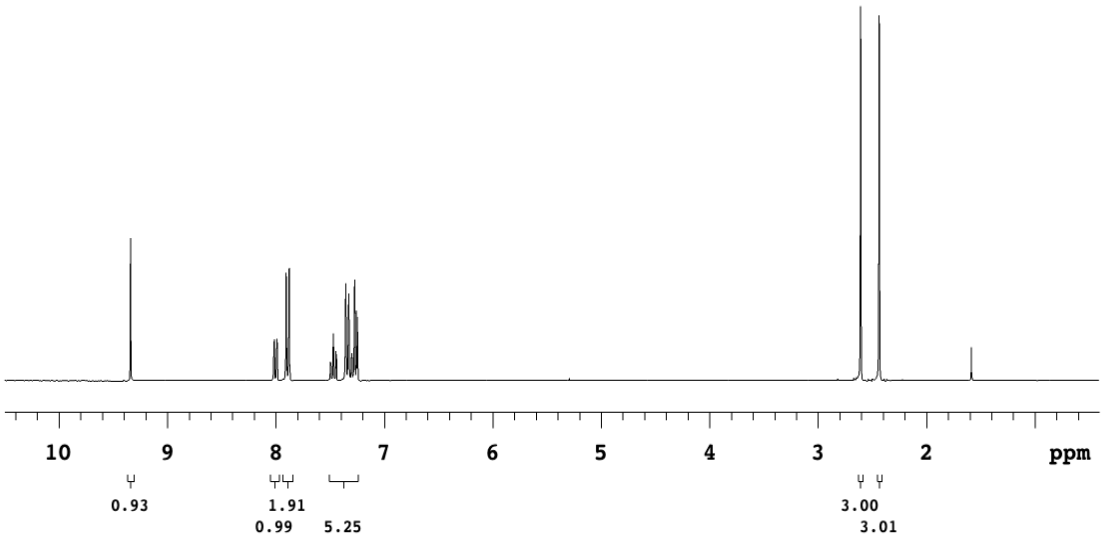
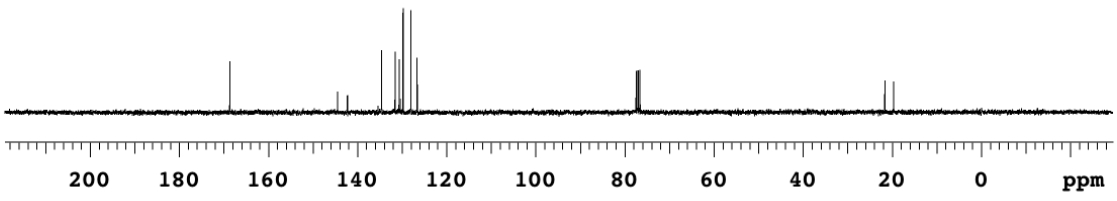
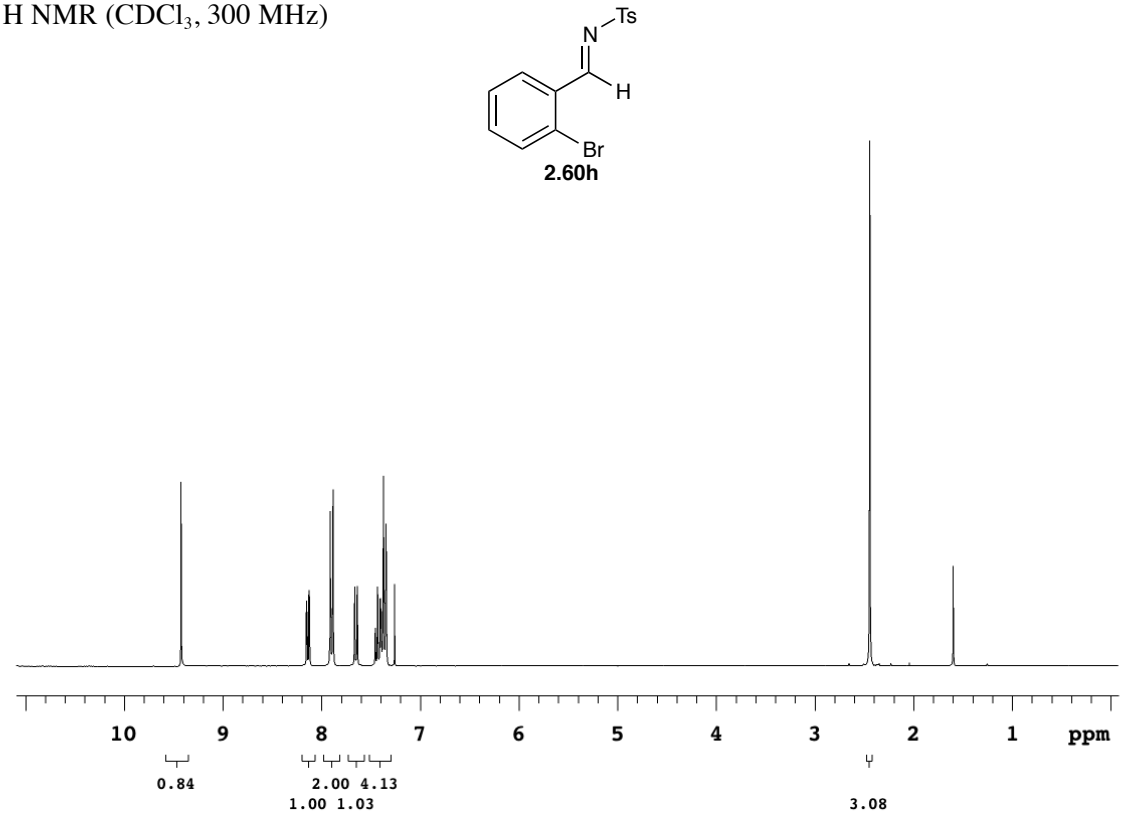


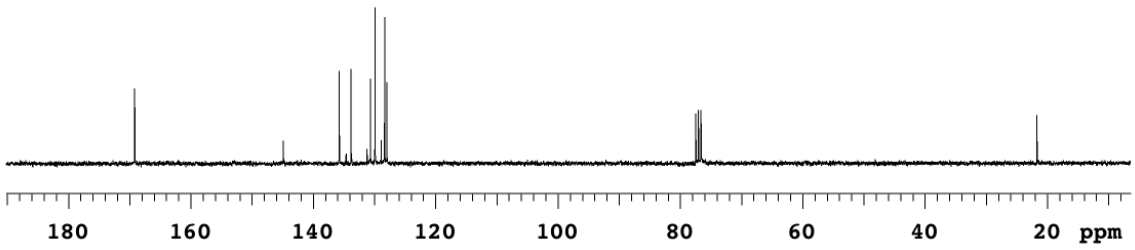
^{13}C NMR ($CDCl_3$, 75 MHz)



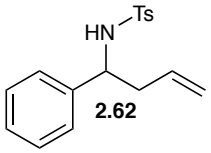
H NMR ($CDCl_3$, 300 MHz)

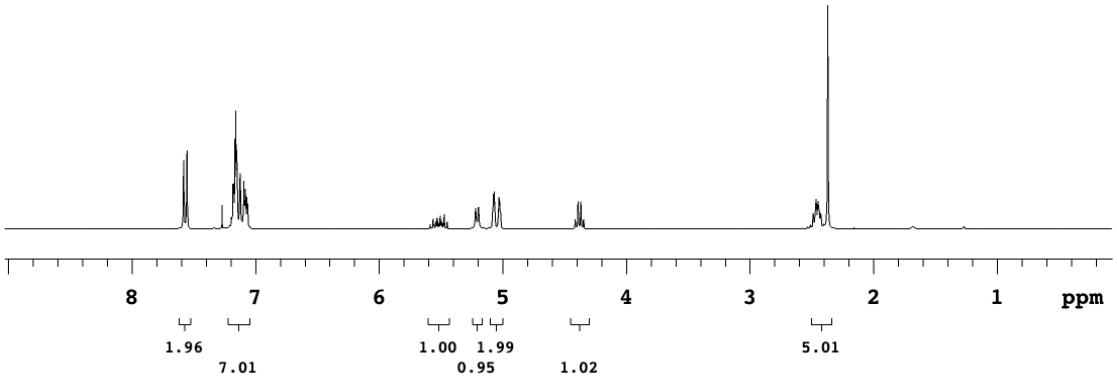


^{13}C NMR ($CDCl_3$, 75 MHz)

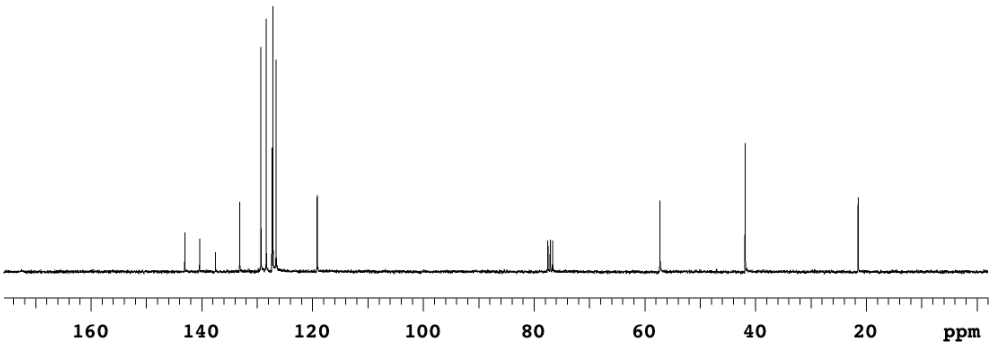


^{1}H NMR ($CDCl_3$, 300 MHz)

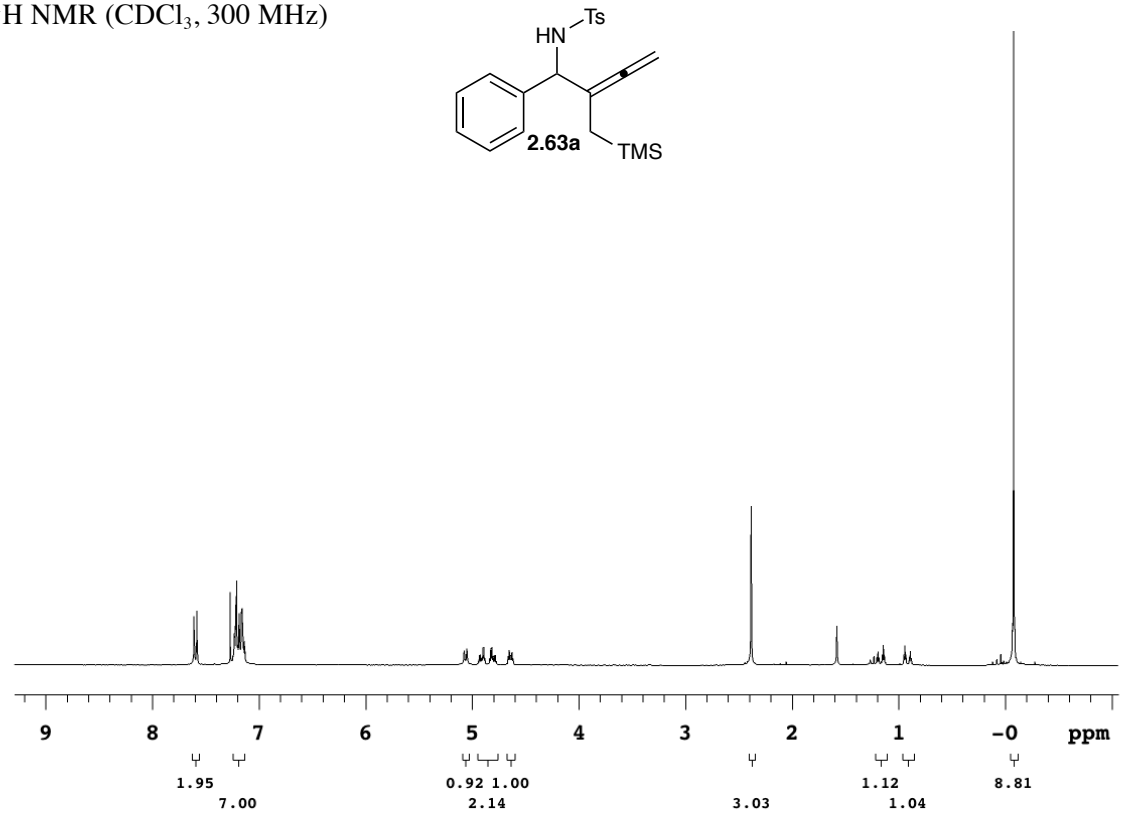




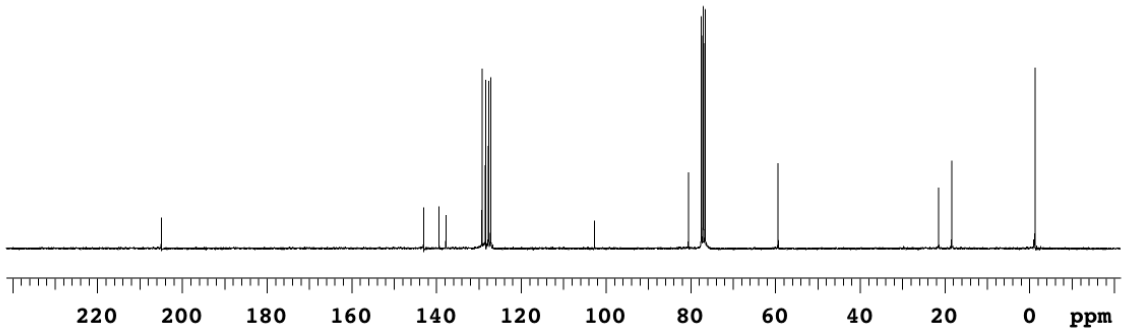
^{13}C NMR ($CDCl_3$, 75 MHz)



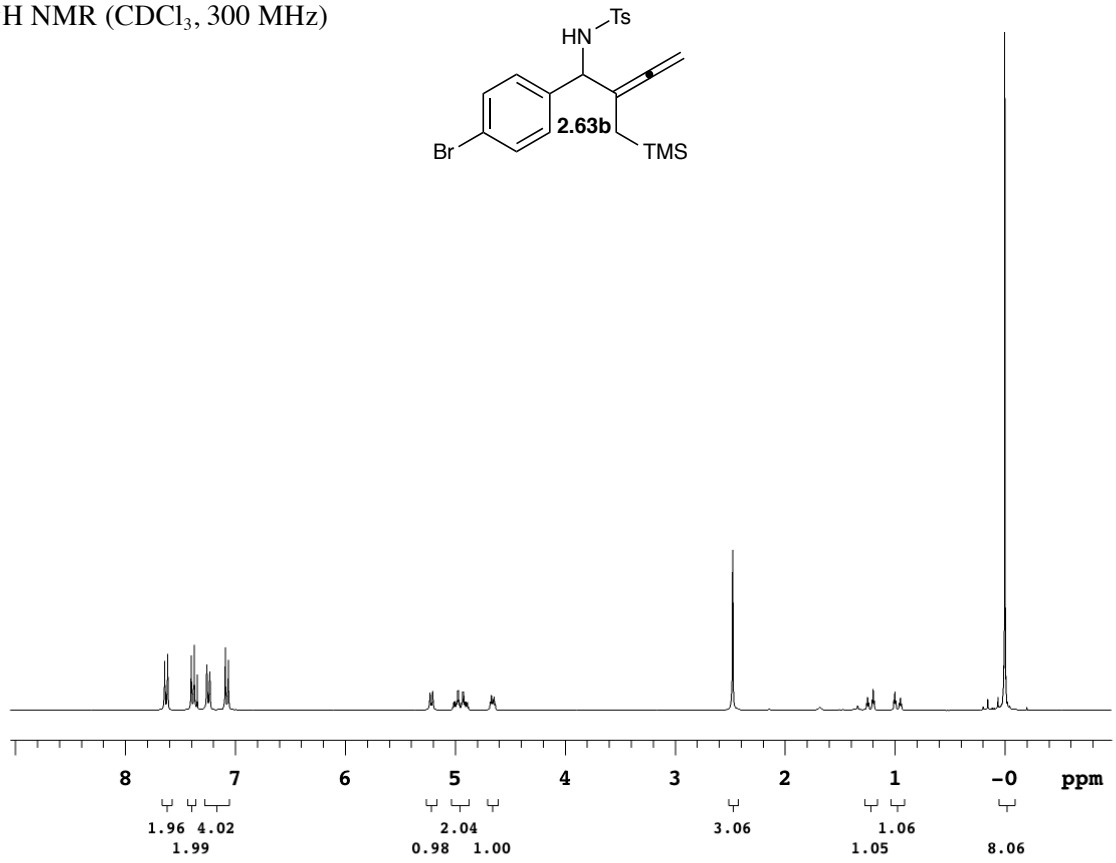
^{1}H NMR ($CDCl_3$, 300 MHz)



^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



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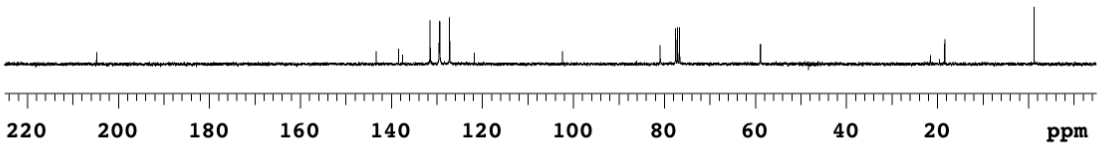

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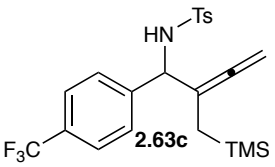

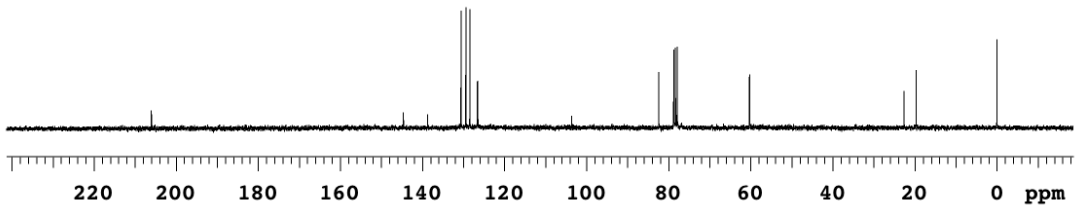

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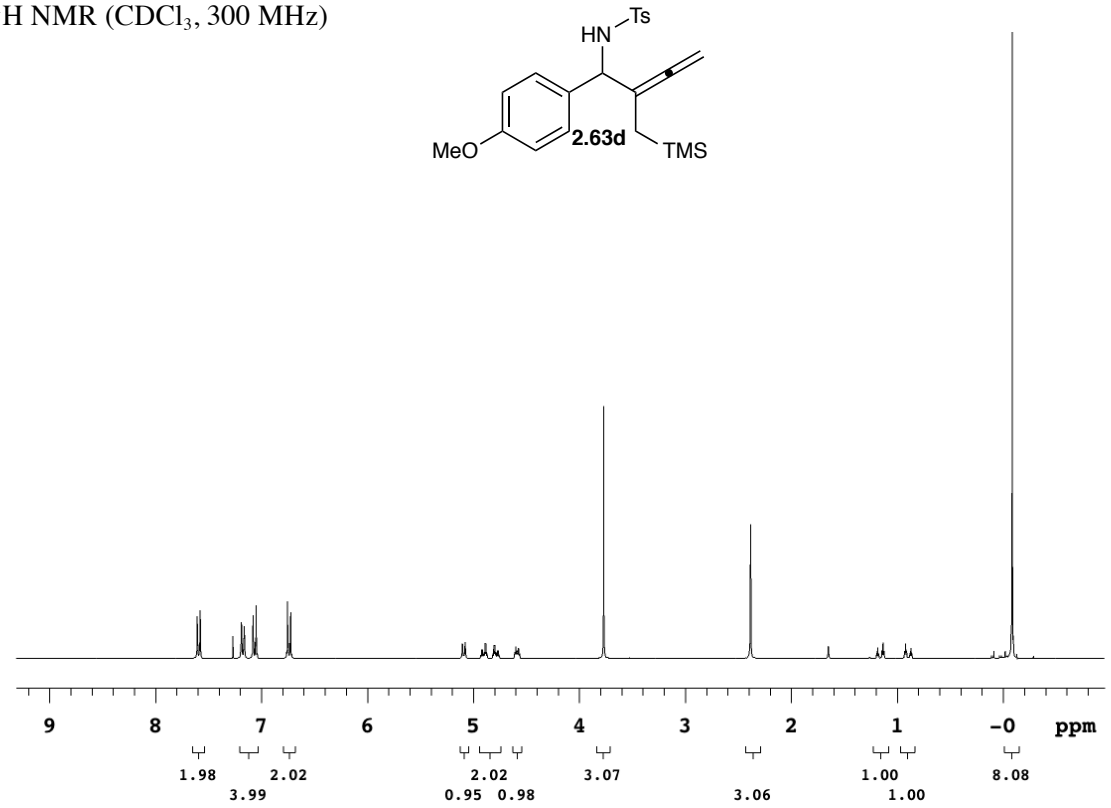

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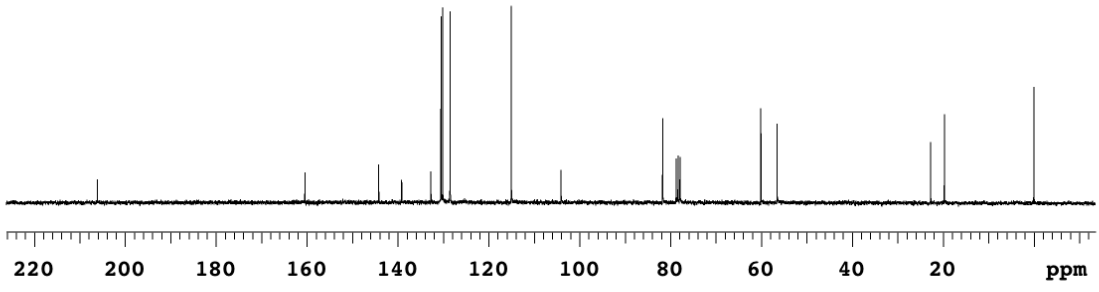

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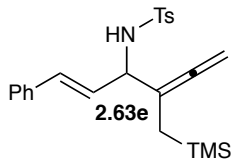
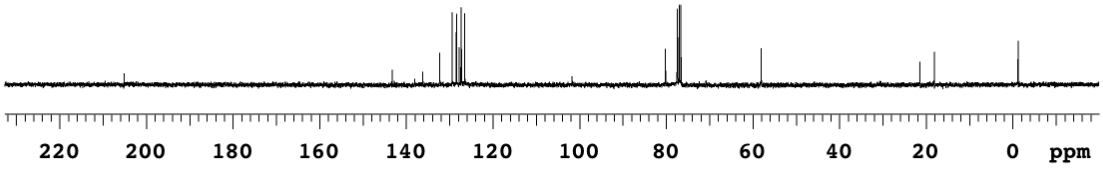
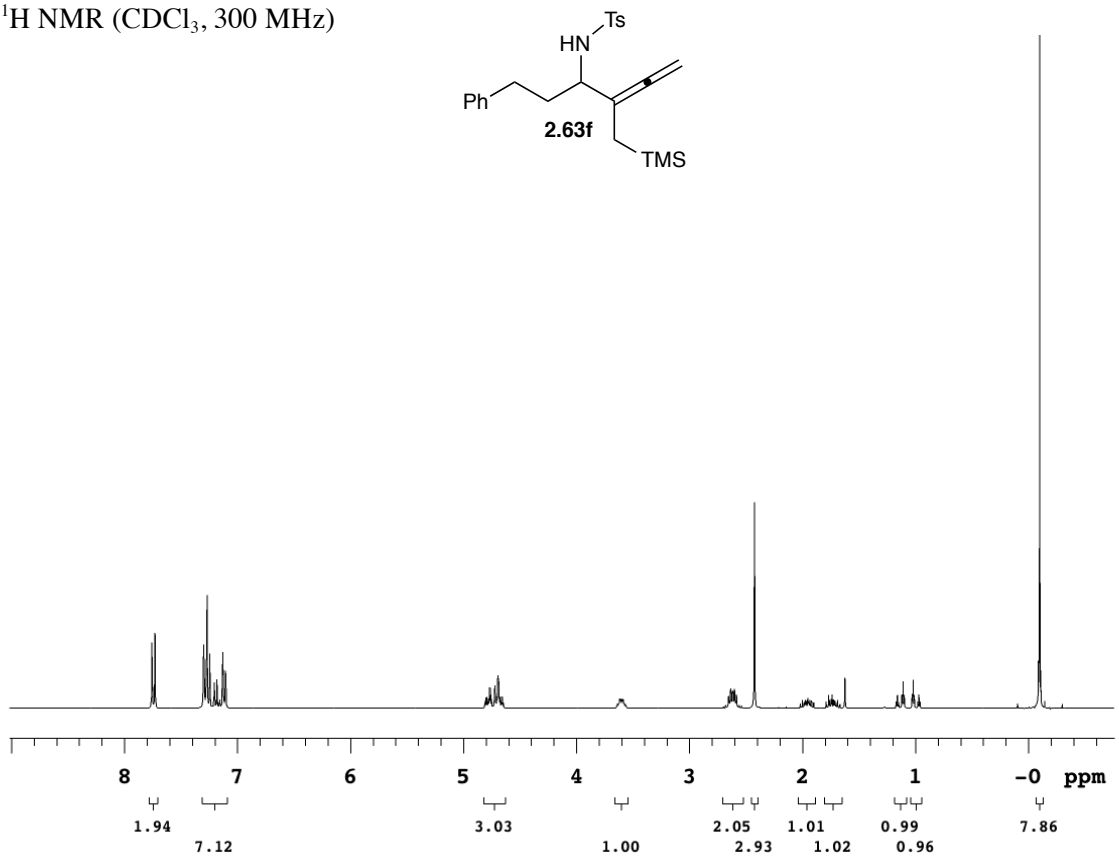


^{13}C NMR ($CDCl_3$, 75 MHz)



^{1}H NMR ($CDCl_3$, 300 MHz)



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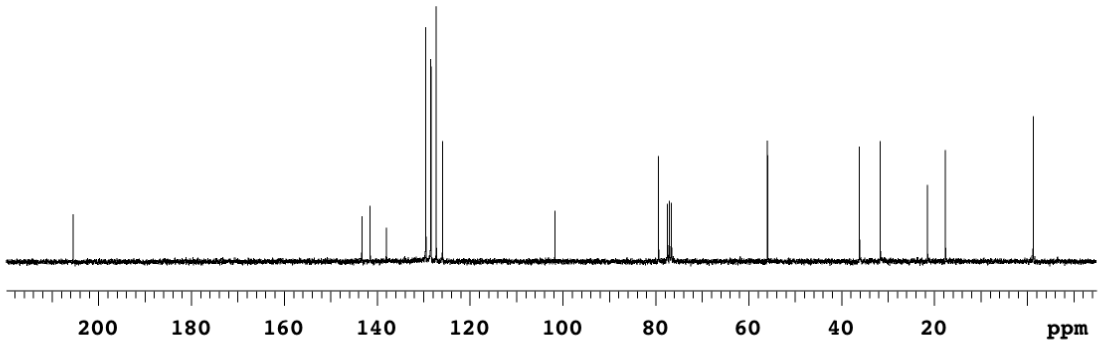

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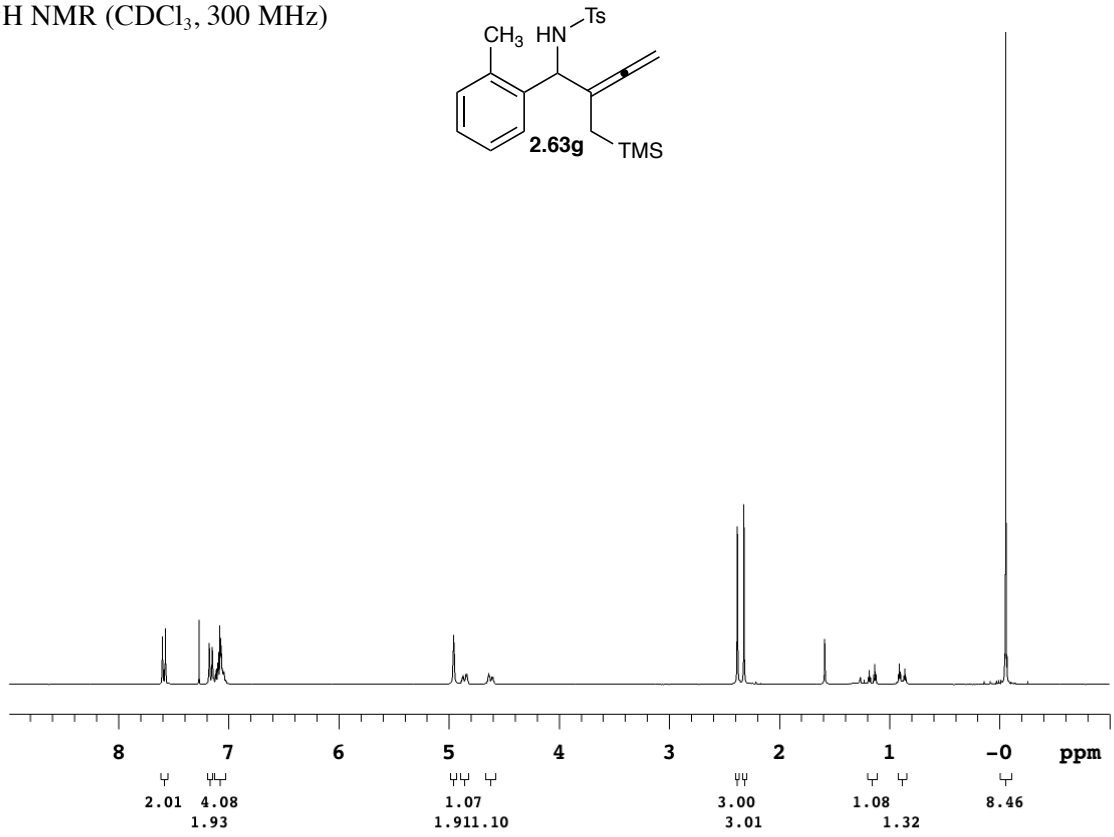

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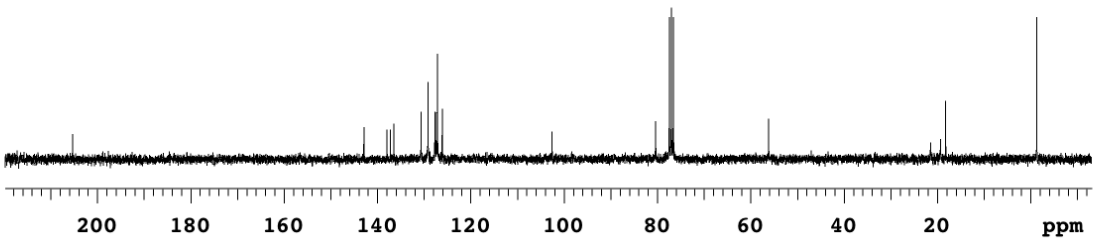

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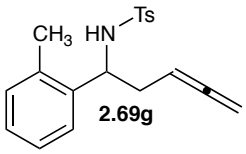

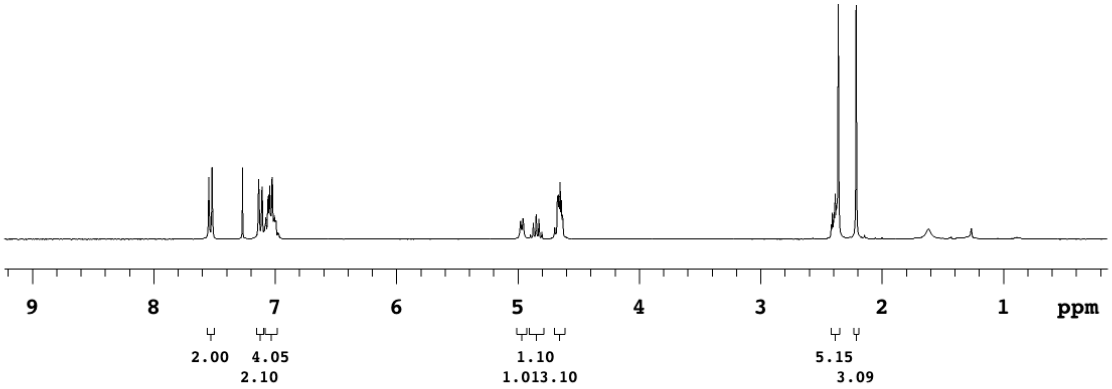

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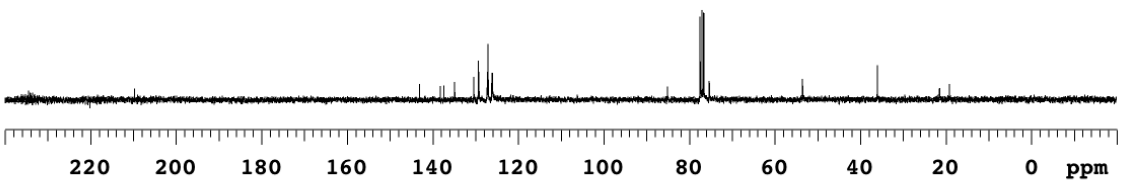

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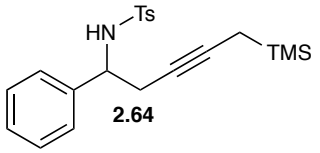

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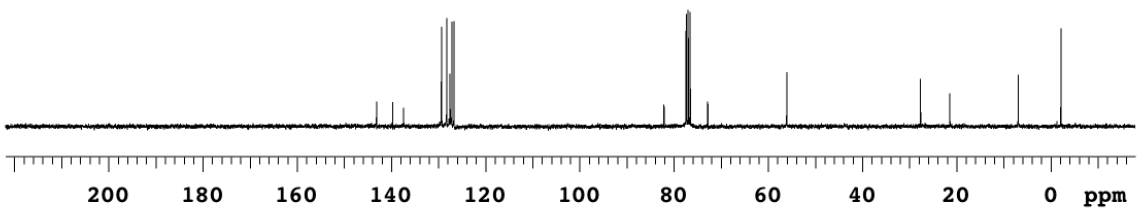

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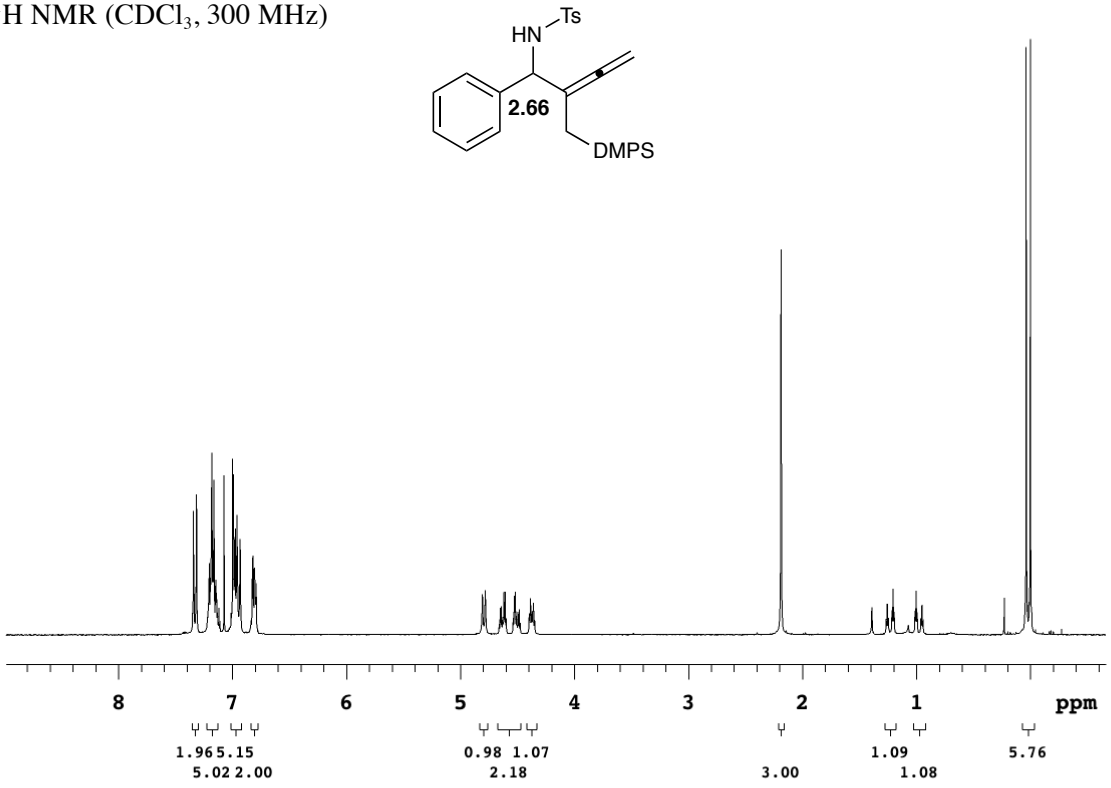

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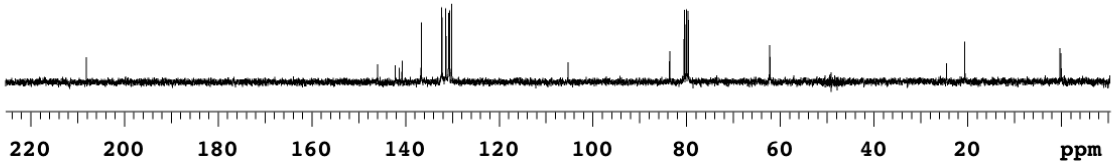

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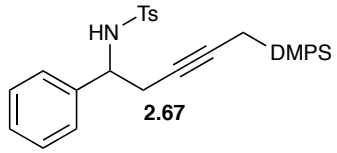

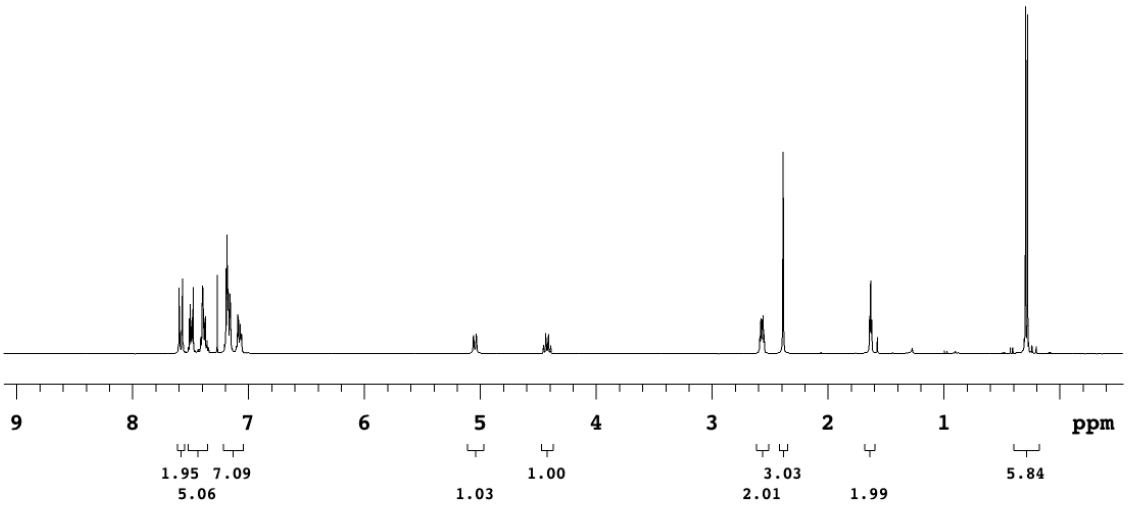

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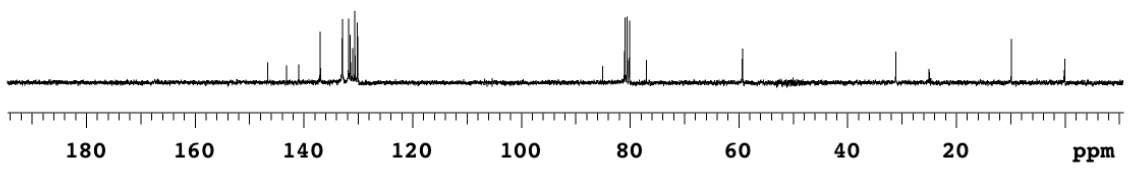

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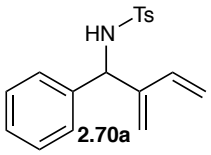

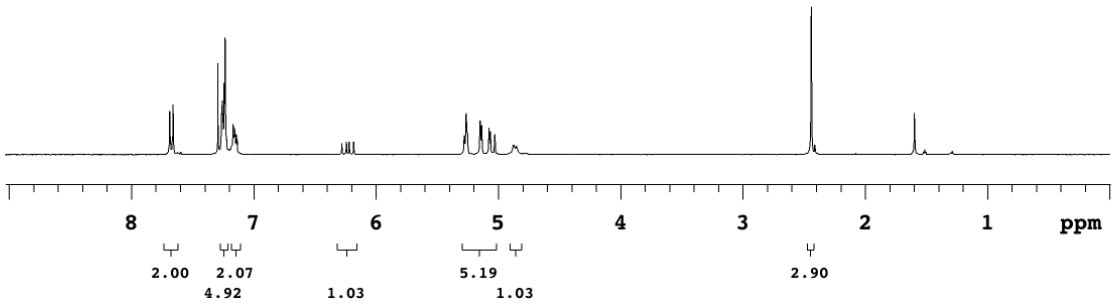

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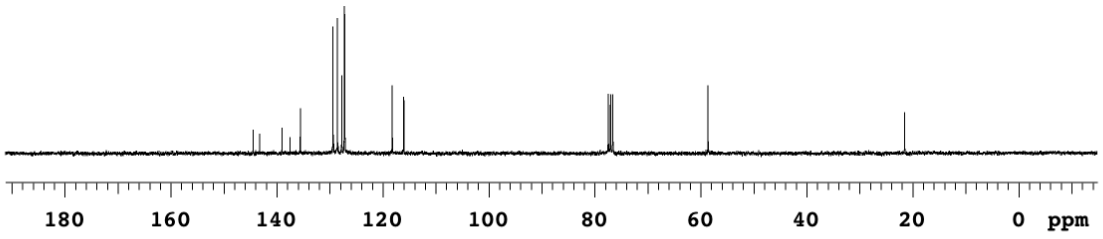

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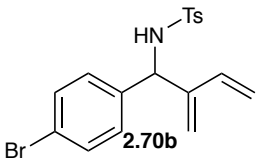

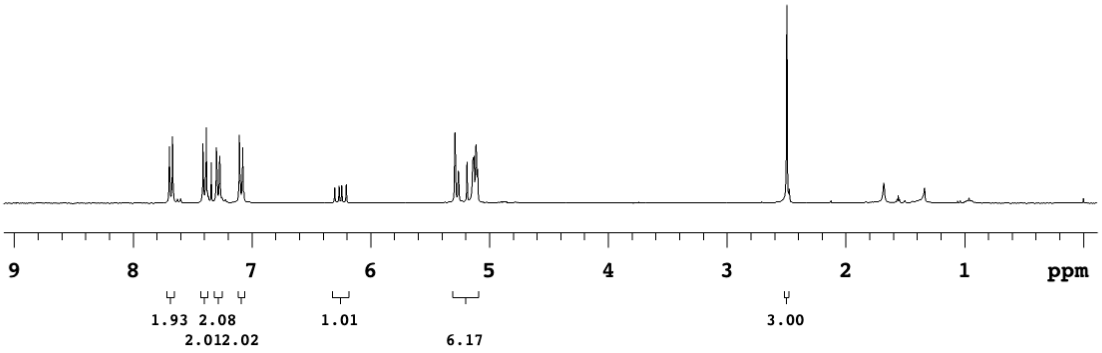

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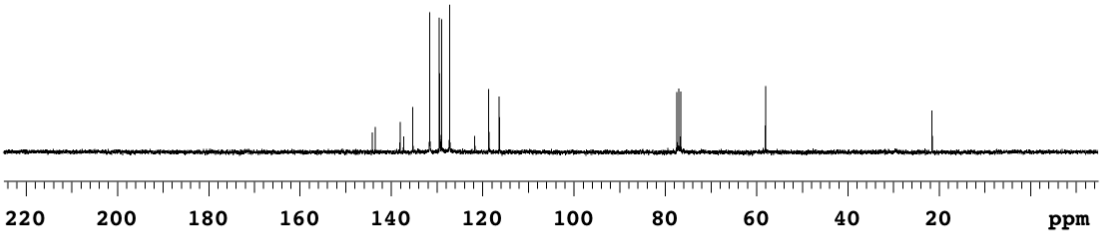

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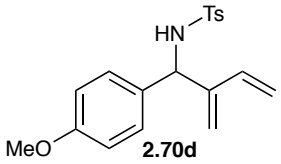
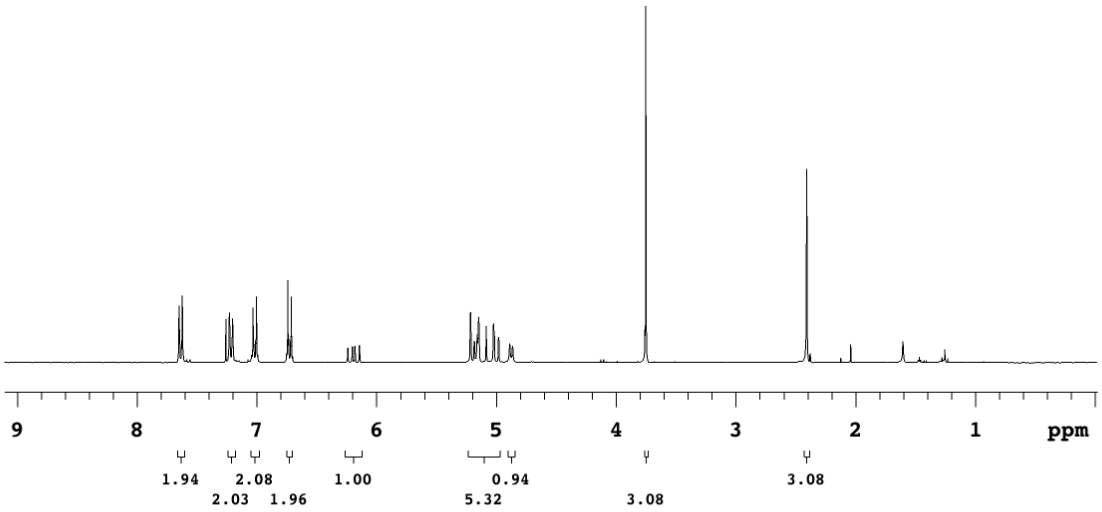


2.70d



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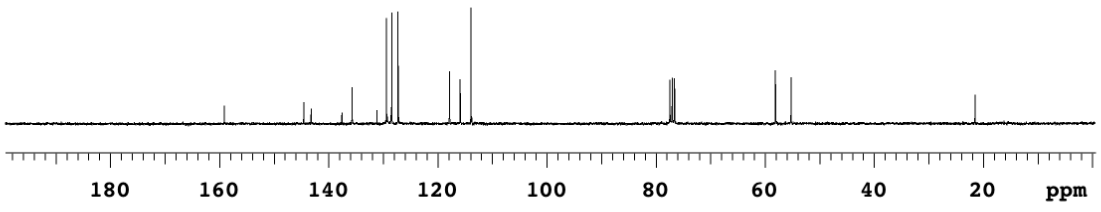

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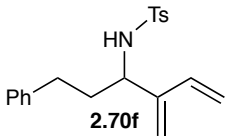
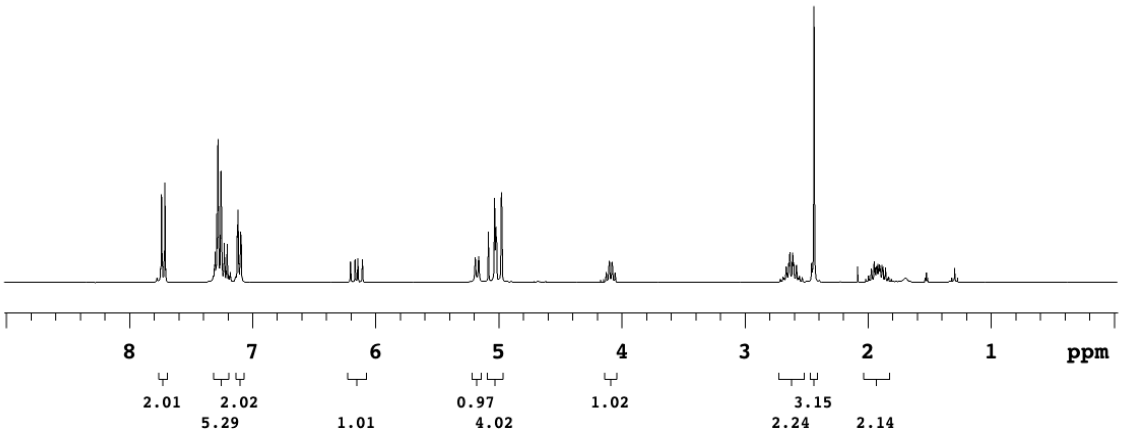
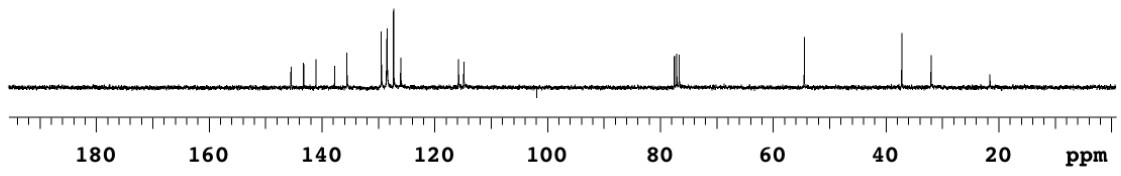




^{13}C NMR ($CDCl_3$, 75 MHz)



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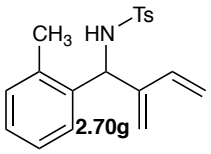

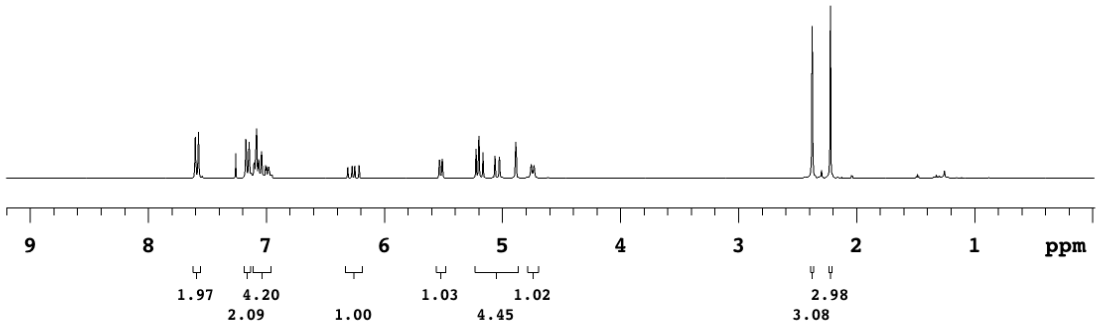

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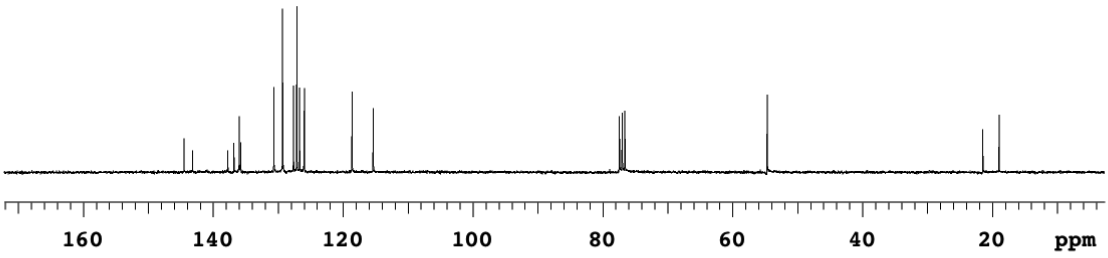

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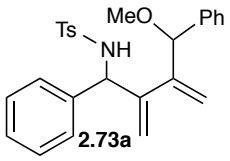

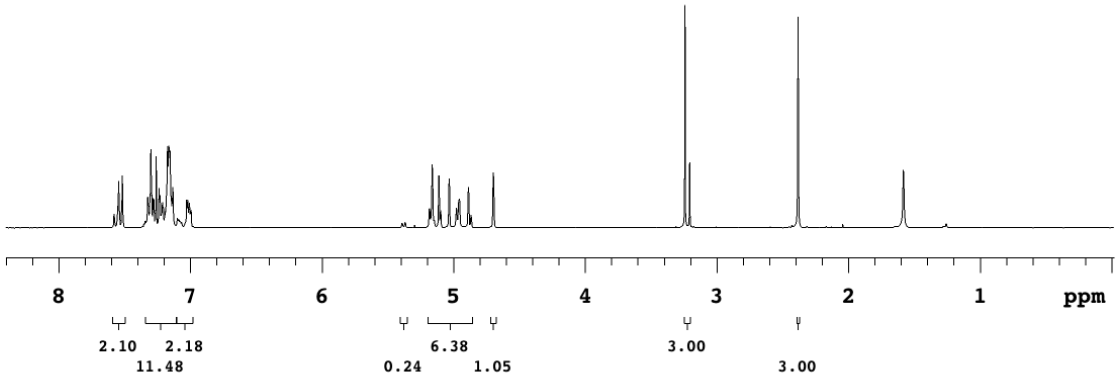

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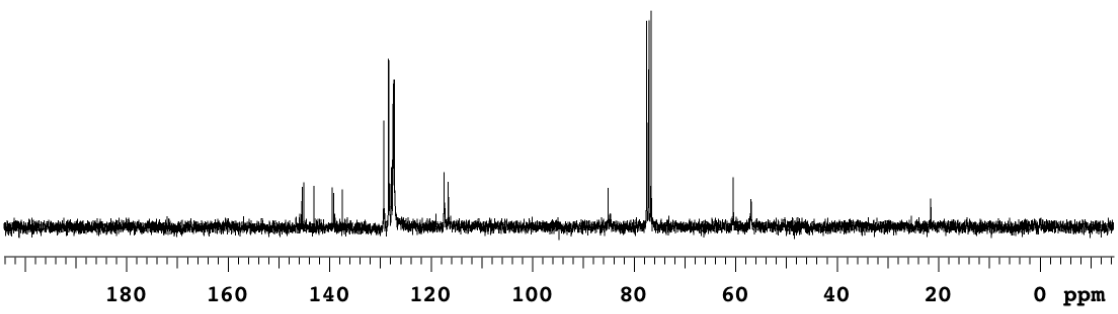

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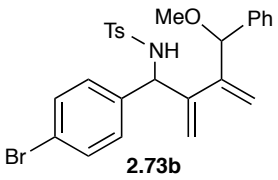
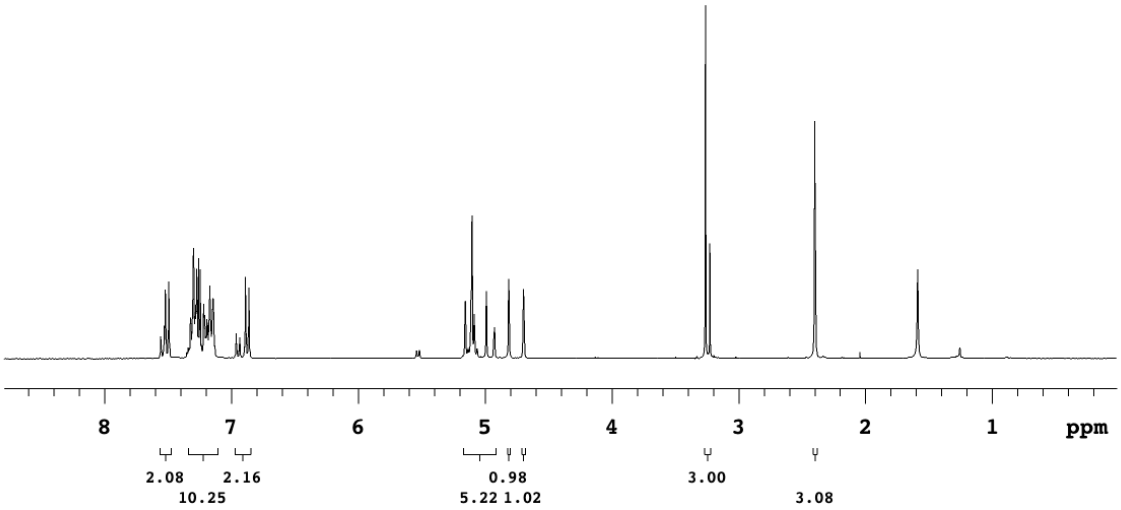


2.73b



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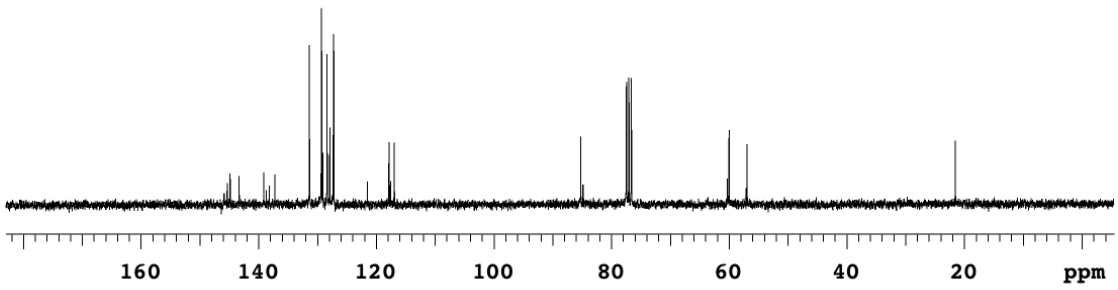
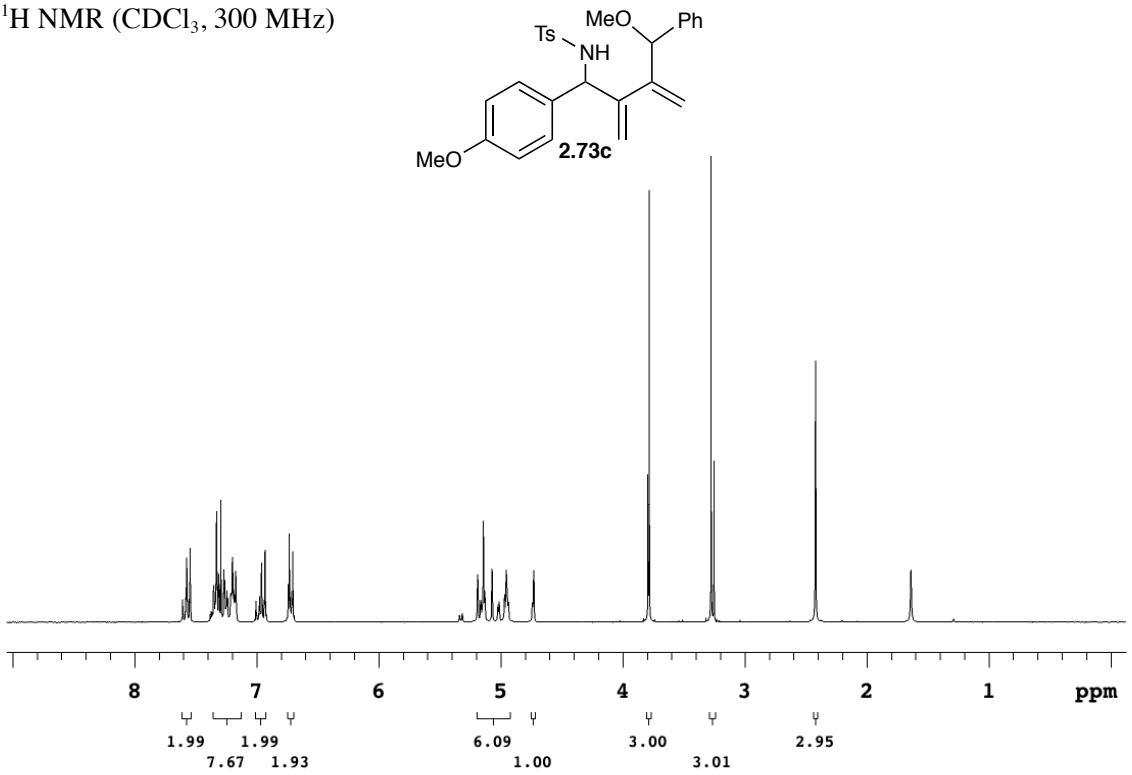
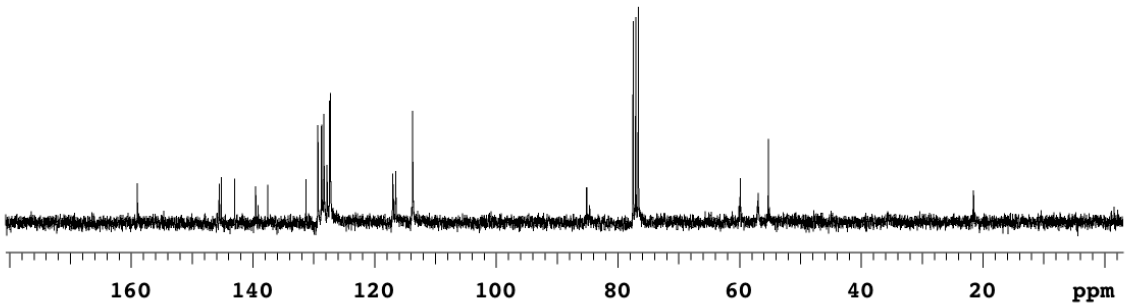


^{1}H NMR ($CDCl_3$, 300 MHz)



^{13}C NMR ($CDCl_3$, 75 MHz)



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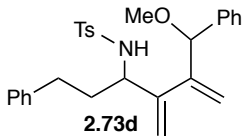
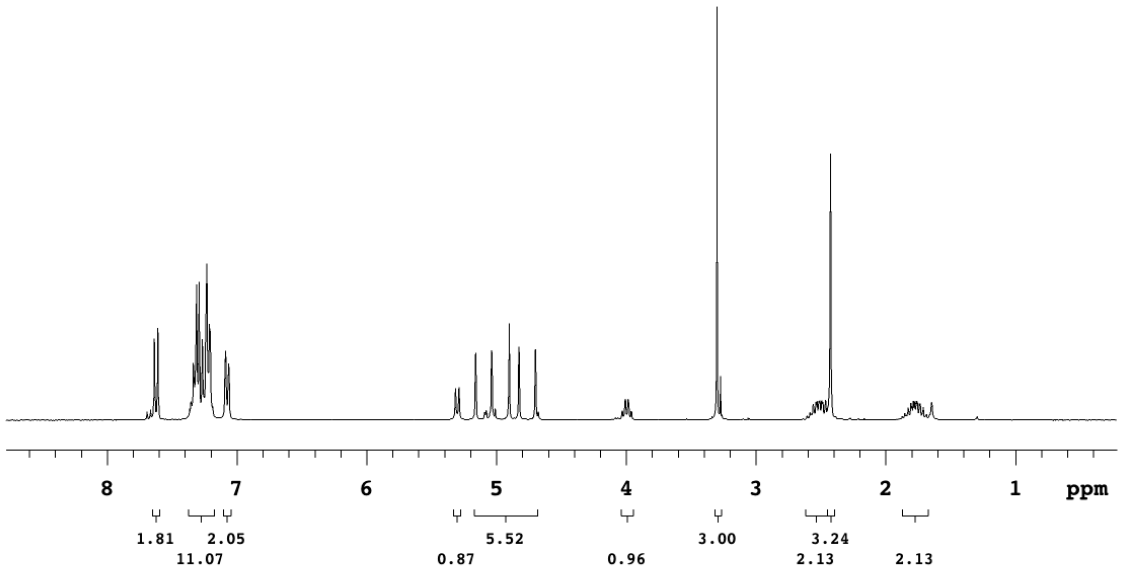


2.73d



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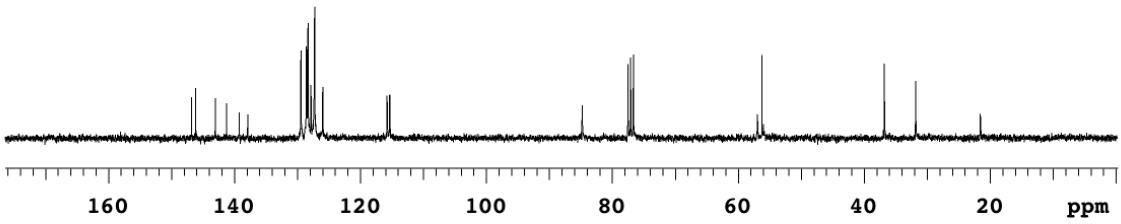

VITA

María Durán Galván received her Bachelor of Science degree in chemistry from Instituto Tencnológico y de Estudios Superiores de Monterrey at Monterrey, México in 2004. She entered the chemistry program at Texas A&M University in May 2005 and received her Doctor of Philosophy degree in August 2011.

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